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(54) Title: SEMAPHORIN RECEPTORS

(57) Abstract

The invention provides methods and compositions relating to two classes of semaphorin receptors, SR1 and SR2. The polypeptides may be produced recombinantly from transformed host cells from the disclosed SR encoding nucleic acids or purified from human cells. The invention provides isolated SR hybridization probes and primers capable of specifically hybridizing with the disclosed SR genes, SR-specific binding agents such as specific antibodies, and methods of making and using the subject compositions in diagnosis, therapy and in the biopharmaceutical industry.

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Semaphorin Receptors

This Application is a continuing application under 35USC120 of USSN 08/889,458 filed July 8, 1997 by Marc Tessier-Lavigne, Zhigang He and Hang Chen and entitled *Semaphorin Receptors*.

The research carried out in the subject application was supported in part by grants from the National Institutes of Health. The government may have rights in any patent issuing on this application.

INTRODUCTION

Field of the Invention

The field of this invention is proteins involved in nerve cell guidance.

Background

During nervous system development, axons migrate along prescribed pathways in the embryo to reach their appropriate synaptic targets (reviewed in Tessier-Lavigne and Goodman, 1996). One mechanism that contributes to accurate pathfinding is chemorepulsion, the guidance of axons away from non-target regions by diffusible chemorepellent factors secreted by non-target cells. Experiments in which axons are confronted with non-target tissues in tissue culture and are repelled by these tissues at a distance have demonstrated the existence of diffusible chemorepellent activities for numerous axonal classes (Pini, 1993; Fitzgerald et al., 1993; Colamarino and Tessier-Lavigne, 1995; Tamada et al., 1995; Guthrie and Pini, 1995; Shirasaki et al., 1996) as well as for migrating neuronal cells (Hu and Rutishauser, 1996). At the molecular level, two families of guidance cues, the netrin and semaphorin families, have been shown to comprise members that can function as chemorepellents. In Caenorhaditis elegans, the netrin UNC-6 is thought to repel axons that migrate away from the netrin source since these axons are misrouted at a certain frequency in *unc-6* mutants; this presumed repulsion appears to be mediated by the candidate receptors UNC-5 and UNC-40, which are members of the immunoglobulin superfamily (Hedgecock et al., 1990; Leung-

Hagesteijn et al, 1992; Hamelin et al., 1993; Wadsworth et al., 1996; Chan et al., 1996). Similarly, in vertebrates netrin-1 can repel subsets of motor axons that migrate away from a source of netrin-1 (Colamarino and Tessier-Lavigne, 1994; Varela-Echavarria et al., 1997), a process which might involve vertebrate homologues of UNC-5 and UNC-40, which have been shown to be netrin-binding proteins (Leonardo et al., 1997; Ackermann et al., 1997; Keino-Masu et al., 1996).

The semaphorins are a large family of structurally diverse secreted and transmembrane proteins characterized by the presence of a conserved ~500 amino acid semaphorin domain at their amino termini (reviewed in Kolodkin, 1996). The family was first described and implicated in axon guidance through antibody perturbation studies in insects (Kolodkin et al., 1992; Kolodkin et al., 1993). The connection of this family to chemorepulsion was made with the purification of chicken collapsin-1 as a factor that can cause collapse of sensory growth cones when added acutely in cell culture (Luo et al., 1993). Collapsin-1 and its mammalian homologues (Semaphorin III, also known as Semaphorin D) are secreted semaphorins that possess in addition to the semaphorin domain an immunoglobulin domain and a highly basic carboxy-terminal domain (Luo et al., 1993; Kolodkin et al., 1993; Messersmith et al., 1995; Püschel et al., 1995). When presented chronically from a point source, collapsin-1/SemaIII/D (hereafter referred to as SemaIII) can repel sensory and sympathetic axons and has been implicated in patterning sensory axon projections into the ventral spinal cord (Messersmith et al., 1995; Püschel et al., 1995, 1996; Behar et al., 1996; Shepherd et al., 1997). Sema E, which is structurally-related to SemaIII, has also been reported to repel sympathetic axons in culture (cited in Varela-Echavarria and Guthrie, 1997). In Drosophila, the secreted semaphorin SemaII has been implicated as an inhibitor of axon terminal branch formation (Matthes et al., 1995). However, the mechanisms through which semaphorins produce their repellent or inhibitory actions have not been determined.

To elucidate the mechanisms through which semaphorin proteins produce their repulsive actions on axons, we have sought to identify binding proteins for semphorins on the surfaces of sensory axons. Here we identify two classes of semaphorin receptors, SR1 and SR2, expressed by axons whose function is required for the collapse-inducing and repulsive actions of semaphorins.

SUMMARY OF THE INVENTION

The invention provides methods and compositions relating to isolated semaphorin receptor class 1 and 2 (SR1 and SR2, collectively SR) polypeptides, related nucleic acids, polypeptide domains thereof having SR-specific structure and activity, and modulators of SR function, particularly semaphorin-binding activity. SR polypeptides can regulate cell, especially nerve cell, function and morphology. The polypeptides may be produced recombinantly from transformed host cells from the subject SR polypeptide encoding nucleic acids or purified from mammalian cells. The invention provides isolated SR hybridization probes and primers capable of specifically hybridizing with the disclosed SR genes, SR-specific binding agents such as specific antibodies, and methods of making and using the subject compositions in diagnosis (e.g. genetic hybridization screens for SR transcripts), therapy (e.g. SR inhibitors to promote nerve cell growth) and in the biopharmaceutical industry (e.g. as immunogens, reagents for isolating other Srs, reagents for screening chemical libraries for lead pharmacological agents, etc.).

BRIEF DESCRIPTION OF THE FIGURES

Figure 1A-1B. Structure of rat and human SR1.

(A) Alignment of the amino acid sequences of mouse, rat and human SR1s.

(B) Diagram displaying the modular structure of SR1s conserved among different species, and the five SR1 domains (a1, a2, b1, b2, c). S: signal peptide; C1r/s, complement C1r/s homology domain (CUB domain); FV/VIII, regions of homology to coagulation factors V and VIII, the DDR tyrosine kinase, and MFGPs; MAM, MAM domain; TM, transmembrane domain.

Figure 2. Equilibrium Binding of Fusion Proteins of AP and different portions of SemaIII to SR1-Expressing cells.

Figure 3. Alignment of the amino acid sequences of neuropilin-1 (SR1) and neuropilin-2 (SR2). Alignment of the mouse neuropilin-1 (m-npn-1), mouse neuropilin-2 (m-npn-2) and human neuropilin-2 (h-npn-2) sequences was performed using the Clustal V program. Different domains of the molecules, named according to Kawakami et al. (1996) (see Figure 2A), are indicated. The a0 isoform of neuropilin-2 (see Figure 2) was used to

create the alignment.

Figure 4A-4C. Domain structure and isoforms of neuropilin-2.
(A) Diagram illustrating the domain structures of mouse neuropilin-1 (Kawakami, et al., 1996) and the full length mouse neuropilin-2(a0) and neuropilin-2(b0) isoforms. s: signal peptide; a1 and a2 domains are CUB domains (Busby and Ingham, 1990; Bork and Beckmann, 1993); b1 and b2 domains show homology to the C1 and C2 domains of coagulation factors V and VIII and of milk fat globular membrane protein; c domain contains a MAM domain, which is found in the metalloendopeptidase meprin and receptor tyrosine phosphatases μ, λ,and κ; TM: transmembrane domain; Cy: cytoplasmic domain. The numbers with arrows indicate percent amino acid identity in the indicated domains. The dashed line and arrow indicate the site in neuropilin-2 where the neuropilin-2a and -2b isoforms diverge; this is also the site of the 5-, 17- and 22- amino acid insertions (see also Figure 2B).
(B) Isoforms of neuropilin-2(a) with 0, 5, 17 and 22 amino acid insertions after amino acid 809 (isoforms 2(a0), 2(a5), 2(a17) and 2(a22), respectively), and of neuropilin-2(b) without and with the 5 amino acid insertion (isoforms 2(b0) and 2(b5), respectively). Shown are the sequences of the insertions, flanked by 3 amino acids N terminal to the insertion (AFA) and 4 amino acids C terminal to the insertions (DEYE in neuropilin-2a, GGTL in neuropilin-2b).
(C) Sequence of neuropilin-2(b0) and partial sequence of human neuropilin-2(b0) from EST (AA25804) in the region where the sequence of neuropilin-2(b0) diverges from that of neuropilin-2(a0). Three amino acids N terminal to the site of divergence (AFA) are shown.

Figure 5A-5B. Equilibrium binding of semaphorin-AP fusion proteins to neuropilin-expressing cells. Transfected or control COS cells were incubated with concentrated media containing the indicated concentrations of semaphorin-AP fusion proteins. AP activity derived from bound fusion proteins was measured colorimetrically at 405 nm; specific binding was obtained after subtraction of background from control cells. Specific binding curves to cells expressing neuropilin-1 (closed circles) or neuropilin-1 (closed squares) are shown for Sema III-AP (A), Sema E-AP (B), and Sema IV-AP (C).

Dissociation constants for interaction with neuropilin-2-expressing cells were 0.29 for Sema E-AP and 0.09 nM for Sema IV-AP.

DETAILED DESCRIPTION OF THE INVENTION

The nucleotide sequences of exemplary natural cDNAs encoding human, rat and mouse SR1 polypeptides are shown as SEQ ID NOS:1, 3 and 5, respectively, and the full conceptual translates are shown as SEQ ID NOS:2, 4 and 6. Natural SR2 cDNAs are found in (a) and (b) forms deriving from two distinct genes, with transcripts of each found in four alternatively spliced forms designated 0, 5, 17 and 22, depending on the size of an insert (below). For example, the nucleotide sequences of exemplary natural cDNAs encoding mouse SR2(a)0, 5, 17 and 22 polypeptides are shown as SEQ ID NOS:9, 11, 13 and 15, respectively, and the full conceptual translates are shown as SEQ ID NOS:10, 12, 14 and 16. Other sequences recited in the Sequence Listing include the nucleotide sequences of exemplary natural cDNAs encoding mouse SR2(b)0 and 5 polypeptides (SEQ ID NOS:21 and 23) and their full conceptual translates (SEQ ID NOS:22 and 24); rat SR2(a)0 polypeptide (SEQ ID NO:7) and its full conceptual translate (SEQ ID NO:8); human SR2(a)0 and 17 polypeptides (SEQ ID NOS:17 and 19) and their full conceptual translates (SEQ ID NOS:18 and 20); and human SR2(b)0 polypeptide (SEQ ID NO:25) and its full conceptual translate (SEQ ID NO:26). The SR polypeptides of the invention include incomplete translates of SEQ ID NOS:1, 3, 7, 9, 11, 13, 15, 17, 19, 21, 23 and 25 and deletion mutants of SEQ ID NOS:2, 4, 8, 10, 12, 14, 16, 18, 20, 22, 24 and 26, which translates and deletion mutants have SR-specific amino acid sequence, binding specificity or function. Preferred translates/deletion mutants comprise at least a 6, preferably at least an 8, more preferably at least a 10, most preferably at least a 12 residue domain of the translates not found in mouse, drosophila or chick neuropilin-1. Other preferred mutants comprise a domain comprising at least one SR2 and/or human specific residue. Such domains are readily discernable from alignments of the disclosed SR1 and SR2 polypeptides, e.g. Figures 1 and 3. For example, human SR1 specific residues include V11, V15, P18, A19, N24, E26, D29, S35, D62, M68, F90, N96, H98, F99, R100, T153, S155, S170, V177, P196, D219, I242, V269, S298, A303, R323, K360, I361, V363, T372, I373, P379, V380, L381, V393, A394, P399, A40, T411, S449, G453, S469, A476, S479, I481, I487, E491, I498, G518, M528, T553, P555, A556, G572, A587, L599,

D601, V634, N667, V669, K672, S674, N717, R737, A755, I756, S805, A813, P820, G835, E838, E855, T916, Q917 and T919.

The subject domains provide SR domain specific activity or function, such as SR-specific cell, especially neuron modulating or modulating inhibitory activity, semaphorin-binding or binding inhibitory activity. SR-specific activity or function may be determined by convenient *in vitro,* cell-based, or *in vivo* assays: e.g. *in vitro* binding assays, cell culture assays, in animals (e.g. gene therapy, transgenics, etc.), etc. Binding assays encompass any assay where the molecular interaction of an SR polypeptide with a binding target is evaluated. The binding target may be a natural intracellular binding target such as a semaphorin, a SR regulating protein or other regulator that directly modulates SR activity or its localization; or non-natural binding target such a specific immune protein such as an antibody, or an SR specific agent such as those identified in screening assays such as described below. SR-binding specificity may assayed by binding equilibrium constants (usually at least about $10^7 M^{-1}$, preferably at least about $10^8 M^{-1}$, more preferably at least about $10^9 M^{-1}$), by the ability of the subject polypeptide to function as negative mutants in SR-expressing cells, to elicit SR specific antibody in a heterologous host (e.g a rodent or rabbit), etc. In any event, the SR binding specificity of the subject SR polypeptides necessarily distinguishes mouse, chick and drosophila neuropilin-1.

For example, the a1, a2, b1, b2, c, TM and Cy domains (Fig.4A) and the polypeptides comprising the inserts shown in Fig. 4B and 4C are all shown to exhibit SR specific binding. Similarly, high throughput screens (e.g. see below) using SR-specific binding agents such as semaIII and anti-SR antibodies are used to readily demonstrate SR-specific binding agents in a wide variety of deletion mutants of the disclosed SR polypeptides. For example, human SR1 peptides with assay demonstrable SR-specific activity include: SEQ ID NO:2, residues 24-34; SEQ ID NO:2, residues 57-68; SEQ ID NO:2, residues 85-111; SEQ ID NO:2, residues 147-155; SEQ ID NO:2, residues 166-178; SEQ ID NO:2, residues 288-299

SEQ ID NO:2, residues 354-366; SEQ ID NO:2, residues 368-690; SEQ ID NO:2, residues 697-415; SEQ ID NO:2, residues 595-615; SEQ ID NO:2, residues 671-689; SEQ ID NO:2, residues 911-919. Human SR2 peptides with assay demonstrable SR-specific activity include: SEQ ID NO:20, residues 14-35; SEQ ID NO:20, residues 261-

278; SEQ ID NO:20, residues 285-301; SEQ ID NO:20, residues 471-485; SEQ ID NO:20, residues 616-628; SEQ ID NO:20, residues 651-685; SEQ ID NO:20, residues 682-696; SEQ ID NO:20, residues 719-745; SEQ ID NO:20, residues 802-825; SEQ ID NO:20, residues 815-830; SEQ ID NO:20, residues 827-839; and SEQ ID NO:20, residues 898-929.

The claimed SR polypeptides are isolated or pure: an "isolated" polypeptide is unaccompanied by at least some of the material with which it is associated in its natural state, preferably constituting at least about 0.5%, and more preferably at least about 5% by weight of the total polypeptide in a given sample and a pure polypeptide constitutes at least about 90%, and preferably at least about 99% by weight of the total polypeptide in a given sample. A polypeptide, as used herein, is an polymer of amino acids, generally at least 6 residues, preferably at least about 10 residues, more preferably at least about 25 residues, most preferably at least about 50 residues in length. The SR polypeptides and polypeptide domains may be synthesized, produced by recombinant technology, or purified from mammalian, preferably human cells. A wide variety of molecular and biochemical methods are available for biochemical synthesis, molecular expression and purification of the subject compositions, see e.g. Molecular Cloning, A Laboratory Manual (Sambrook, *et al.* Cold Spring Harbor Laboratory), Current Protocols in Molecular Biology (Eds. Ausubel, *et al.*, Greene Publ. Assoc., Wiley-Interscience, NY) or that are otherwise known in the art.

The invention provides binding agents specific to the claimed SR polypeptides, including natural intracellular binding targets, etc., methods of identifying and making such agents, and their use in diagnosis, therapy and pharmaceutical development. For example, specific binding agents are useful in a variety of diagnostic and therapeutic applications, especially where disease or disease prognosis is associated with improper or undesirable axon outgrowth or orientation. Novel SR-specific binding agents include SR-specific receptors, such as somatically recombined polypeptide receptors like specific antibodies or T-cell antigen receptors (see, e.g Harlow and Lane (1988) Antibodies, A Laboratory Manual, Cold Spring Harbor Laboratory), semaphorins and other natural intracellular binding agents identified with assays such as one-, two- and three-hybrid screens, non-natural intracellular binding agents identified in screens of chemical libraries such as described below, etc. Agents of particular interest modulate SR function, e.g.

semaphorin-mediated cell modulation. For example, a wide variety of inhibitors of SR activity may be used to cell function involving SR, especially SR-semaphorin interations. Exemplary SR activity inhibitors include SR-derived peptide inhibitors, esp. dominant negative deletion mutants, etc., see Experimental, below.

Accordingly, the invention provides methods for modulating cell function comprising the step of modulating SR activity, e.g. by contacting the cell with an SR inhibitor. The cell may reside in culture or in situ, i.e. within the natural host. Preferred inhibitors are orally active in mammalian hosts. For diagnostic uses, the inhibitors or other SR binding agents are frequently labeled, such as with fluorescent, radioactive, chemiluminescent, or other easily detectable molecules, either conjugated directly to the binding agent or conjugated to a probe specific for the binding agent.

The amino acid sequences of the disclosed SR polypeptides are used to back-translate SR polypeptide-encoding nucleic acids optimized for selected expression systems (Holler et al. (1993) Gene 136, 323-328; Martin et al. (1995) Gene 154, 150-166) or used to generate degenerate oligonucleotide primers and probes for use in the isolation of natural SR-encoding nucleic acid sequences ("GCG" software, Genetics Computer Group, Inc, Madison WI). SR-encoding nucleic acids used in SR-expression vectors and incorporated into recombinant host cells, e.g. for expression and screening, transgenic animals, e.g. for functional studies such as the efficacy of candidate drugs for disease associated with SR-modulated cell function, etc.

The invention also provides nucleic acid hybridization probes and replication / amplification primers having a SR cDNA specific sequence comprising SEQ ID NO:1, 3, 7, 9, 11, 13, 15, 17, 19, 21, 23, or 25, and sufficient to effect specific hybridization thereto (i.e. specifically hybridize with SEQ ID NO:1, 3, 7, 9, 11, 13, 15, 17, 19, 21, 23, or 25, respectively, in the presence of mouse, drosophila and chick neuropilin cDNA. Such primers or probes are at least 12, preferably at least 24, more preferably at least 36 and most preferably at least 96 bases in length. Demonstrating specific hybridization generally requires stringent conditions, for example, hybridizing in a buffer comprising 30% formamide in 5 x SSPE (0.18 M NaCl, 0.01 M $NaPO_4$, pH7.7, 0.001 M EDTA) buffer at a temperature of 42°C and remaining bound when subject to washing at 42°C with 0.2 x SSPE; preferably hybridizing in a buffer comprising 50% formamide in 5 x SSPE buffer at a temperature of 42°C and remaining bound when subject to washing at

42°C with 0.2 x SSPE buffer at 42°C. SR nucleic acids can also be distinguished using alignment algorithms, such as BLASTX (Altschul *et al.* (1990) Basic Local Alignment Search Tool, J Mol Biol 215, 403-410).

The subject nucleic acids are of synthetic/non-natural sequences and/or are isolated, i.e. unaccompanied by at least some of the material with which it is associated in its natural state, preferably constituting at least about 0.5%, preferably at least about 5% by weight of total nucleic acid present in a given fraction, and usually recombinant, meaning they comprise a non-natural sequence or a natural sequence joined to nucleotide(s) other than that which it is joined to on a natural chromosome. The subject recombinant nucleic acids comprising the nucleotide sequence of SEQ ID NO:1, 3, 7, 9, 11, 13, 15, 17, 19, 21, 23, or 25, or fragments thereof, contain such sequence or fragment at a terminus, immediately flanked by (i.e. contiguous with) a sequence other than that which it is joined to on a natural chromosome, or flanked by a native flanking region fewer than 10 kb, preferably fewer than 2 kb, which is at a terminus or is immediately flanked by a sequence other than that which it is joined to on a natural chromosome. While the nucleic acids are usually RNA or DNA, it is often advantageous to use nucleic acids comprising other bases or nucleotide analogs to provide modified stability, etc.

The subject nucleic acids find a wide variety of applications including use as translatable transcripts, hybridization probes, PCR primers, diagnostic nucleic acids, etc.; use in detecting the presence of SR genes and gene transcripts and in detecting or amplifying nucleic acids encoding additional SR homologs and structural analogs. In diagnosis, SR hybridization probes find use in identifying wild-type and mutant SR alleles in clinical and laboratory samples. Mutant alleles are used to generate allele-specific oligonucleotide (ASO) probes for high-throughput clinical diagnoses. In therapy, therapeutic SR nucleic acids are used to modulate cellular expression or intracellular concentration or availability of active SR.

The invention provides efficient methods of identifying agents, compounds or lead compounds for agents active at the level of a SR modulatable cellular function. Generally, these screening methods involve assaying for compounds which modulate SR interaction with a natural SR binding target such as a semaphorin. A wide variety of assays for binding agents are provided including labeled *in vitro* protein-protein binding assays, immunoassays, cell based assays, etc. The methods are amenable to automated,

cost-effective high throughput screening of chemical libraries for lead compounds. Identified reagents find use in the pharmaceutical industries for animal and human trials; for example, the reagents may be derivatized and rescreened in *in vitro* and *in vivo* assays to optimize activity and minimize toxicity for pharmaceutical development.

In vitro binding assays employ a mixture of components including an SR polypeptide, which may be part of a fusion product with another peptide or polypeptide, e.g. a tag for detection or anchoring, etc. The assay mixtures comprise a natural intracellular SR binding target. In a particular embodiment, the binding target is a semaphorin polypeptide. While native full-length binding targets may be used, it is frequently preferred to use portions (e.g. peptides) thereof so long as the portion provides binding affinity and avidity to the subject SR polypeptide conveniently measurable in the assay. The assay mixture also comprises a candidate pharmacological agent. Candidate agents encompass numerous chemical classes, though typically they are organic compounds; preferably small organic compounds and are obtained from a wide variety of sources including libraries of synthetic or natural compounds. A variety of other reagents may also be included in the mixture. These include reagents like salts, buffers, neutral proteins, e.g. albumin, detergents, protease inhibitors, nuclease inhibitors, antimicrobial agents, etc. may be used.

The resultant mixture is incubated under conditions whereby, but for the presence of the candidate pharmacological agent, the SR polypeptide specifically binds the cellular binding target, portion or analog with a reference binding affinity. The mixture components can be added in any order that provides for the requisite bindings and incubations may be performed at any temperature which facilitates optimal binding. Incubation periods are likewise selected for optimal binding but also minimized to facilitate rapid, high-throughput screening.

After incubation, the agent-biased binding between the SR polypeptide and one or more binding targets is detected by any convenient way. Where at least one of the SR or binding target polypeptide comprises a label, the label may provide for direct detection as radioactivity, luminescence, optical or electron density, etc. or indirect detection such as an epitope tag, etc. A variety of methods may be used to detect the label depending on the nature of the label and other assay components, e.g. through optical or electron density, radiative emissions, nonradiative energy transfers, etc. or indirectly detected with

antibody conjugates, etc.

A difference in the binding affinity of the SR polypeptide to the target in the absence of the agent as compared with the binding affinity in the presence of the agent indicates that the agent modulates the binding of the SR polypeptide to the SR binding target. For example, in the cell-based assay also described below, a difference in SR-dependent modulation of axon outgrowth or orientation in the presence and absence of an agent indicates the agent modulates SR function. A difference, as used herein, is statistically significant and preferably represents at least a 50%, more preferably at least a 90% difference.

The following experimental section and examples are offered by way of illustration and not by way of limitation.

EXPERIMENTAL

Expression cloning of a cDNA encoding a SemaIII-binding protein

To facilitate isolation of SemaIII-binding proteins through expression cloning, we fused the coding region of SemaIII to that of alkaline phosphatase (AP), a readily detectable histochemical reporter, and expressed the resulting chimeric protein in human embryonic kidney 293 cells. This protein could be detected by Western blotting in conditioned medium from these cells as a major band of ~180 kDa, consistent with the combined sizes of SemaIII and AP; a few smaller products, apparently degradation products, were also detected in this medium. When this medium was applied to dissociated sensory neurons from dorsal root ganglia (DRG), AP-reactivity could be detected on the axons and cell bodies of neurons from E14 DRG but not E18 DRG. AP alone, also expressed in 293 cells, did not bind cells at either age. The binding of Sema-AP to E14 but not E18 DRG cells is not unexpected since at E14 DRG axons are beginning to project into the spinal cord and can be repelled by a factor, likely Sema III, secreted by the ventral spinal cord (Fitzgerald et al., 1993; Messersmith et al., 1995; Shepherd et al., 1997), whereas by E18 they are no longer repelled by ventral spinal cord tissue (Fitzgerald et al., 1993), perhaps reflecting a downregulation of their responsiveness to SemaIII.

To identify SemaIII-binding proteins on E14 rat DRG neurons, a cDNA expression library was constructed in a COS cell expression vector using cDNA derived

from E14 DRG tissue (see Experimental Procedures). Pools of ~1000-2000 cDNA clones from the library were transfected into COS cells and screened for the presence of cells that bound SemaIII-AP. A positive pool was identified after screening 70 pools. After three rounds of screening subpools from this pool, a single cDNA encoding a SemaIII-AP binding activity was identified. COS-7 cells transfected with this cDNA specifically bound SemaIII-AP but not AP or a netrin-Fc fusion protein (Keino-Masu et al., 1996).

Nucleotide sequencing of the entire 5 kB cDNA insert revealed a single long open reading frame predicted to encode a protein (rat semaphorin receptor 1, rSR1) of 921 amino acids with sequence similarity with mouse, chicken and Xenopus neuropilin (Takagi et al., 1991, 1995; Kawakami et al., 1996). We further isolated a cDNA encoding a human homolog of our semphorin binding protein (hSR1) from a fetal human brain library (see Experimental Procedures), and Figure 1A shows an alignment of the full conceptual translated amino acid sequences of our rat and human proteins with mouse neuropilin. The rat and human proteins share a high degree of sequence homology with the mouse protein (97% and 93% identity at the amino acid level, respectively), and are predicted to have the domain structure previously described for neuropilins from other species, including a short but highly conserved cytoplasmic domain (Figure 1B).

We next performed coimmunoprecipitation experiments to test whether the binding of SemaIII-AP to COS-7 cells expressing rSR1 reflected a direct interaction between SemaIII and rSR1or required cellular factors made by the COS-7 cells. For this purpose we constructed a soluble version of the ectodomain of rSR1 fused to AP. A myc-tagged SemaIII protein could be precipitated by beads conjugated with this SR-AP fusion, but not with beads conjugated with a control fusion protein, c-kit-AP (Flanagan and Leder, 1990), indicating a direct interaction between the SR1 ectodomain and SemaIII.

SR1 binds both the semaphorin and the C-terminal domains of SemaIII

SemaIII consists of a signature semaphorin domain, a single immunoglobulin (Ig) domain, and a carboxy terminal (C) domain that is rich in basic residues (Luo et al., 1993; Kolodkin et al., 1993; Messersmith et al., 1995; Püschel et al., 1995). The conservation of semaphorin domains among different semaphorin family members (reviewed in Tessi-Lavigne and Goodman, 1996; Kolokin, 1996) suggests the potential importance of this domain for function. The functions of the other two domains are unknown, although the basic nature of the C domain has suggested a role for this domain in mediating

interactions with cell surfaces or the extracellular matrix (Luo et al., 1993). To determine which domain of SemaIII mediates the interaction between SemaIII and SR1, constructs encoding various fusions of AP to different portions of SemaIII were expressed in COS cells. Media conditioned by these cells were applied to COS-7 cells expressing SR1 to test for binding of AP fusion proteins ; in positive control experiments, binding was observed with medium containing full length SemaIII-AP but not AP alone . Binding was also observed with an AP fusion protein comprising the semaphorin and Ig domains (AP-SI) and a fusion protein comprising just the semaphorin domain (AP-S), but not with a fusion protein comprising a truncated semaphorin domain, suggesting that the integrity of the semaphorin domain is required for binding. Surprisingly, binding was also observed with AP fusion proteins comprising only the C domain (AP-C) and a fusion protein comprising the Ig and C domains. These results provide evidence that both the semaphorin and the C domains of SemaIII can bind SR1. The binding of the C domain does not appear to reflect a non-specific interaction arising from the basic nature of the C domain since we found that the C terminal domain of netrin-1 (Serafini et al., 1994), which is also highly basic but does not share any sequence homology with the SemaIII C domain, did not bind SR1.

We next measured the binding affinity of the full-length and two of the truncated fusion ligands (AP-S and AP-C) to cells expressing SR1 in equilibrium binding experiments, based on the relative amounts of AP activity in the supernatant and bound to cells (Figure 2). One limitation of these experiments is that we used partially purified conditioned media (see Experimental Procedures) which in the case of SemaIII-AP and AP-C contain both the full length fusion proteins as well as truncated forms that are presumed to arise by proteolysis. For each of these fusions, the estimated dissociation constant would be accurate only if all the degradation products that possess AP activity bind with the same affinity as the intact fusion protein; this is unlikely to be the case since the media contain protein species that appear to correspond to AP or fragments of AP, which do not bind SR1. This limitation does not apply to AP-S since in this case only the full length species is found in the supernatant; the estimated dissociation constant should therefore accurately reflect the affinity of AP-S for the SR1-expressing cells. With these caveats, we found that the specific binding curves of SemaIII-AP, AP-S and AP-C to cells expressing SR1 showed saturation and could be fitted with the Hill equation (Figures 2A-

C). Predicted values for the dissociation constants (Kd) for SemaIII-AP, AP-S and AP-C binding to SR1-expressing cells were 0.325 nM, 1.45 nM, and 0.84 nM, respectively. For comparison, in the collapse assay , a half maximal collapse response is observed with conditioned medium containing 0.44 nM SemaIII-AP. This value is comparable to the estimated Kd for the interaction of SemaIII-AP with SR1. These results support the role of an interaction of SemaIII with SR1 on DRG axons in causally mediating collapse.

For these experiments, control 293-EBNA cells or 293-EBNA cells stably expressing rat SR1 were treated for 90 min with concentrated conditioned media containing the indicated concentrations of SemaIII-AP (A), AP-S (B), or AP-C (C). After washing six times in HBHA buffer, the cells were lysed and endogenous AP activity was heat-inactivated. AP activity derived from the bound recombinant AP fusion proteins was measured colorimetrically (optical density at 405 nm). Specific binding was determined by subtraction of values obtained from binding to SR1-expressing cells and to control cells; values obtained in this way were fitted to the Hill equation. Insets in Fig. 2 show raw data (circles, total binding to SR1-expressing cells; triangles, total binding to control cells). Kd values for the interactions of SemaIII-AP, AP-S and AP-C with SR1 were 55.3 $\pm$ 6.5 ng/ml, 218.6 $\pm$ 11.0 ng/ml, and 67.2 $\pm$ 3.0 ng/ml, respectively (1 nM corresponds to 170 ng/ml, 150 ng/ml, and 80 ng/ml for SemaIII-AP, AP-S and AP-C, respectively). Bars indicated s.e.m. for triplicates. Hill coefficients for SemaIII-AP, AP-S and AP-C were 1.51 $\pm$ 0.24, 1.70 $\pm$ 0.10, and 1.44 $\pm$ 0.07, respectively.

SR1 function is required for the repulsive action of SemaIII

We next raised antibodies to a portion of the SR1 ectodomain for use in tests of the functional role of SR1 in mediating responses to SemaIII (see Experimental Procedures). To verify the potential usefulness of the antiserum, we first examined whether it could detect SR1 protein on axons. The spatial and temporal pattern of expression of SR1 detected with this antiserum in transverse sections of rat embryos at spinal levels corresponded to the sites of *SR1* gene expression detected by in situ hybridization, and matched the pattern previously observed in mouse and chick embryos (Kawakami et al., 1995; Takagi et al., 1995). At E14, when afferent fibers of DRG neurons start to penetrate the dorsal spinal cord (Windle and Baxter, 1936; Smith, 1983; Altman and Bayer, 1994; Snider et al., 1992; Zhang et al., 1994), *SR1* transcripts were found in the DRG as well as in the ventral and dorsal spinal cord, and corresponding

immunoreactivity for SR1 protein was detected on sensory and motor axons, as well as in the dorsal spinal cord. SR1 immunoreactivity could also be detected with this antiserum on the axons and growth cones of E14 rat DRG neurons in culture, as previously shown for neuropilin with chick DRG axons (Takagi et al., 1995). At E18, much lower levels of *SR1* transcripts were detected in DRG and the ventral horn (see also Kawakami et al., 1995; Takagi et al., 1995 for similar results with neuropilin in mice and chickens). The timing of expression in DRG is consistent with the pattern of SemaIII-AP binding to E14 and E18 DRG cells in culture and with what might be expected of a SemaIII receptor (see Fitzgerald et al., 1993; Messersmith et al., 1995; and discussions therein)

Protein A-purified anti-SR1 antiserum was used to test the involvement of SR1 in mediating the function of SemaIII. Inclusion of the antiserum in the culture medium inhibited the repulsive effect of SemaIII-AP and SemaIII on E14 rat DRG axons in collagen gel cultures in a dose-dependent manner, whereas preimmune IgG, also purified on protein A, did not inhibit the repulsion. To verify that this neutralizing effect was due to antibodies directed against SR1 in the antiserum, aliquots of the antiserum were subjected to immunodepletion by incubation with beads conjugated with the portion of the SR1 ectodomain used to make the antiserum (depleted antiserum) or with control beads (mock-depleted antiserum). The mock-depleted antiserum still detected the SR1 ectodomain-AP fusion protein by Western blotting and was still capable of blocking the inhibitory effect of SemaIII-AP. In contrast, the depleted antiserum did not detect the SR1 ectodomain-AP fusion protein by Western blotting and did not block the inhibitory activity of SemaIII-AP, consistent with the hypothesis that the starting antiserum blocks SemaIII-AP activity by interfering with SR1 function. To rule out the possibility that the antiserum to SR1 affected a general mechanism required for axonal repulsion, the same protein A-purified antiserum was tested for its effect on netrin-mediated repulsion of trochlear motor axons (Colamarino and Tessier-Lavigne, 1995), a group of axons that can also be repelled by SemaIII (Serafini et al., 1996; Varela-Echavaria et al., 1997). The anti-SR1 antiserum stained these axons but did not block the repulsive effect of netrin-1 on these axons, consistent with a specific involvement of SR1 in SemaIII-mediated repulsion.

SR1 function is also required for the collapse-inducing effect of SemaIII

In addition to steering DRG axons away when presented chronically from a point

source, SemaIII can also induce collapse of DRG growth cones when added acutely and uniformly to growth cones in culture (Luo et al., 1993). We therefore examined whether the anti-SR1 antiserum could affect the activity of SemaIII in the collapse assay. The anti-SR1 antiserum inhibited collapse of E14 rat DRG growth cones elicited by SemaIII-AP or SemaIII-myc; the blocking effect showed a dose-dependence that was similar to that observed for the block of repulsion (Table 1). As expected, the mock-depleted antiserum also blocked the collapse, whereas the depleted antiserum did not. To test the specificity of this blockade, we took advantage of the fact that lysophosphatidic acid (LPA) can also cause collapse of DRG growth cones (Jalink et al., 1994). Neither the preimmune serum nor the anti-SR1 antiserum inhibited the collapse of DRG growth cones induced by LPA, consistent with the hypothesis that the antiserum blocks SemaIII-induced collapse by specifically inhibiting SR1 function.

Cloning of a cDNA encoding SR2

To identify additional members of the SR family, we designed PCR primers which would selectively amplify rat cDNA molecules containing both the CUB the MAM motifs of SR1. A single cDNA (SEQ ID NO:7) encoding an 936 amino acid SR1 homolog, designated SR2 (SEQ ID NO:8) was identified. With these data, we were able to identify and composite ESTs in public databases to generate a cDNA sequence encoding hSR2. CDNA's comprising this clone are also isolated from a fetal human brain library (see Experimental Procedures). SR-specific function, including semaphorin binding and neuron axon outgrowth and/or orientation modulating activity are demonstrated as described herein for SR1 polypeptides.

SR1 is a SemaIII receptor

Neuropilin is a transmembrane protein initially identified by Fujisawa and colleagues as an epitope recognized by a monoclonal antibody (A5) that labels specific subsets of axons in the developing Xenopus nervous system (Takagi et al., 1987; Fujisawa et al., 1989; Takagi et al., 1991). Neuropilin comprises in its extracellular domain two so-called CUB motifs, which are found in the noncatalytic regions of the complement components C1r and C1s and several metalloproteinases (for review see Bork and Beckmann, 1993). These domains are followed in neuropilin by two domains with significant similarity to many proteins, including the C1 and C2 domains of coagulation factors V and VIII (Toole et al., 1984; Jenny et al., 1987), the milk fat globule

membrane proteins (MFGPs) (Stubbs et al., 1990), and the discoidin domain receptor (DDR) (Johnson et al., 1993; Sanchez et al., 1994). More proximal to the transmembrane region is a MAM domain, a type of motif implicated in protein-protein interactions (Beckmann and Bork, 1993). The cytoplasmic domain of neuropilin is short (40 amino acids) and does not possess obvious motifs, but is highly conserved among Xenopus, mouse and chick (Takagi et al., 1995; Kawakami et al., 1996). In the developing nervous systems of these three species, neuropilin is expressed in dynamic fashion by a variety of different classes of axons (including motor and sensory axons) as they project to their targets (e.g., Takagi et al., 1987, 1991, 1995; Kawakami et al., 1996). Neuropilin can promote neurite outgrowth in vitro (Hirata et al., 1993) and forced expression of neuropilin under control of the β-actin promoter in transgenic mice results in axonal defasciculation (Kitsukawa et al., 1995). The forced ectopic expression of neuropilin also leads to abnormalities in development of the heart and limbs, two of the non-neural regions where neuropilin is expressed, which has suggested a role for neuropilin in organogenesis outside the nervous system (Kitsukawa et al., 1995).

We have identified SR1 and SR2 semaphorin receptors with sequence similarity to the neuropilin proteins. The spatiotemporal expression pattern of SR1 is consistant with SR1's role as a SemaIII receptor. In the region of the developing spinal cord, SR1 is most prominently expressed by sensory neurons in the DRG, particularly on their axons in the spinal nerves, the dorsal roots, and the dorsal funiculus and SR1 can also be detected on the growth cones of axons derived from dissociated DRG neurons in culture. The period during which SR1 and neuropilin is expressed by DRG neurons (between E9 and E15.5 in the mouse, decreasing sharply thereafter (Kawakami et al., 1995)) correponds to the timing of projection of SemaIII-responsive DRG axon projections into the spinal cord. During this period, Sema III is expressed at a high level in the ventral spinal cord and has been implicated as a diffusible chemorepellent that prevents inappropriate targeting of NGF-responsive axons that normally terminate in the dorsal spinal cord (Messersmith et al., 1995, Püschel et al., 1995, 1996; Shepherd et al., 1997). Our in situ hybridization studies suggest that SR1 may be expressed in only some populations of rat DRG cells at E14 – possibly the NGF-responsive neurons, which are SemaIII responsive. In addition to developing DRG axons, several other classes of developing axons are repelled by or collapse in response to SemaIII, including

sympathetic axons (Püschel et al., 1996), spinal motor axons (Shepherd et al., 1996; Varela-Echavarria et al., 1997), and many cranial motor axons such as trochlear, trigeminal motor, glossopharyngeal and vagal axons (Serafini et al., 1996; Varela-Echavarria et al., 1997). All of these axons express SR1.

SR1 also plays a role in mediating actions of SemaIII outside the nervous system. SR1, the neuropilins and SemaIII are expressed in a variety of non-neural tissues, including the developing cardiovascular system and limbs (Takagi et al., 1987, 1991, 1995; Kitsukawa et al., 1995; Püschel et al., 1995; Behar et al., 1996). Ectopic expression of m-neuropilin under control of the β-actin promoter in transgenic mice, in addition to causing sprouting and defasciculation of axons, leads to a variety of morphological abnormalities in non-neural tissues including the presence of excess capillaries and blood vessels, dilation of blood vessels, malformed hearts, and extra digits (Kitsukawa et al., 1995; see also, the defects in axonal, heart and skeletal development seen in SemaIII knock-out mice, Behar et al., 1996).

Our experiments have provided evidence that both the C domain and the semaphorin domain of SemaIII can independently bind SR1. The ability of both poles of the full length SemaIII molecule to bind SR1 could provide an explanation for the data suggesting that full length SemaIII has a higher affinity for SR1 than do either of the individual domains alone, since sequential binding of the two domains of each SemaIII molecule to neighboring SR1 molecules in the cell membrane would result in a higher apparent affinity. This observation indicates that signaling in response to SemaIII might be triggered by dimerization of SR1 molecules brought together by single SemaIII molecules; which is also supported by the observation that AP-S and AP-C, the fusions of AP to the semaphorin domain or the C domain, failed to induce repulsion or to cause collapse of DRG axons in vitro.

SR1 contains at its amino terminus two CUB domains, motifs implicated in protein-protein interactions whose structure is predicted to be an antiparallel β-barrel similar to those in two adhesive domains, immunoglobulin-like domains and fibronectin type III repeats (Bork et al., 1993; Bork and Beckmann, 1993). CUB domains in complement C1r/s appear to mediate calcium-dependent tetrameric complex formation between C1r/s dimers, as well as their association with C1q to form the mature C1 complex (Busby and Ingham, 1988, 1990), whereas a CUB domain in the

metalloproteinase Tolloid (a relative of BMP-1) is suggested from genetic evidence to mediate an interaction with the BMP family member decapentaplegic (Childs and O'Connor, 1994; Finelli et al., 1995). In the central portion of the SR1 molecule, the b1 and b2 domains show homology to protein binding domains of coagulation factors V and VIII (Toole et al., 1984; Jenny et al., 1987), MFGF (Larocca et al., 1991) and two receptor protein-tyrosine kinases, DDR (Johnson et al., 1993) and Ptk-3 (Sanchez et al., 1994). Finally, SR1 also possesses a MAM domain, a ~170 amino acid module found in diverse transmembrane proteins (Beckmann and Bork, 1993), which has been suggested to mediate homophilic interactions (Zondag et al., 1995). We found that a truncated form of SR1 which lacks the amino terminal-most 264 amino acids retains the ability to bind SemaIII-AP, indicating that at least one of the semaphorin and C domains of SemaIII may interact with domains b1 or b2 or the MAM domain of SR1. SemaIII may also modulate the interactions of SR1 with other SR1 binding partner. In the repulsion assay the most obvious effect of Sema III is the steering away of DRG axons from a local source of SemaIII, rather than a change in fasciculation patterns (Messersmith et al, 1995). Furthermore, individual growth cones can be induced to collapse in vitro in response to SemaIII (Luo et al., 1993) in a SR1-dependent fashion, indicating a distinct signaling pathway involving SR1 that can be triggered by SemaIII.

The semaphorin family comprises over 20 proteins, secreted and transmembrane, which have been divided into five subfamilies based on sequence and structural similarity (reviewed by Tessier-Lavigne and Goodman, 1996; Kolodkin, 1996). We have found that the secreted semaphorins SemaA, SemaE and SemaIV, which belong to the same subfamily as SemaIII, can all bind SR1, suggesting promiscuity in interactions between SR1 and members of this subfamily of the semaphorin family. The bewildering diversity of semaphorin proteins may mask an underlying simplicity in interactions of these proteins and their receptors, much as the diversity of Eph receptors and ephrin ligands masks simpler binding relations, in which GPI-anchored ligands of the ephrin-A subclass interact primarily and promiscuously with EphA class receptors, and ligands of the ephrin-B subclass interact primarily and promiscuously with EphB class receptors (Gale et al.; 1996; Eph Nomenclature Committee, 1997).

Experimental procedures: Construction and expression of AP fusion proteins

To produce a Sema III-AP fusion protein, the cDNA encoding full-length Sema III

was amplified by PCR and subcloned into APTag-1 (Flanagan and Leder, 1990). From the resulting plasmid, the fragment encoding both Sema III and AP was then transferred to the expression vector pCEP4 (Invitrogen), and used to transfect 293-EBNA cells (Invitrogen). A cell line stably expressing Sema-AP was established after selection with geneticin and hygromycin. Cells were grown to confluence and then cultured in Optimen medium (BRL) for 3 days. The conditioned medium was collected and partially purified using a Centriprep-100 device (Amicon). A construct encoding the ectodomain of SR1 (amino acids 1 to 857) fused to AP was similarly made in pCEP4 and used to derived a stable cell line. Conditioned medium from this line was prepared in the same way.

For other AP fusion proteins, sequences encoding the Sema domain and Ig domain (amino acids 25 to 654), the Sema domain alone (amino acids 25 to 585), a truncated Sema domain (amino acids 25 to 526), the Ig domain and C-domain together (amino acids 586 to 755), or the C-domain alone (amino acids 655 to 755) were amplified by PCR, fused to the sequence encoding AP, and subcloned into cloning sites after the Ig_κ-chain signal sequence of the expression vector pSecTag B (Invitrogen). These resulting constructs were transiently transfected into Cos-1 or Cos-7 cells with Lipofectamine (GIBCO BRL). Conditioned media were collected as described above.

Expression library construction and screening

80 mg of DRG tissue was dissected from two litters of E14 rat embryos (with kind help of K. Wang) and frozen on dry ice. mRNA was isolated from these rat DRGs using a QuickPrep mRNA purification kit (Pharmicia), and used to generate cDNA using a Stratagene cDNA synthesis kit according to manufacturer's instructions, except that the cDNA was size-fractionated using a DNA Size Fractionation Column (GIBCO BRL). Fractions containing cDNA larger than 500 bp were collected and ligated to the EcoRI-XhoI sites of the COS cell expression vector pMT21 (Genetics Institute). Ligated DNA was ethanol precipitated, resuspended in water at 10 ng/μl, electroporated into SURE 2 supercompetent cells (Stratagene) (1 μl DNA to 40 μl bacteria), and the resulting transformants were divided into pools of ~ 1000 to 2000 colonies.

To screen the library, DNA was extracted from the bacteria in each pool using the SNAP miniprep kit (Invitrogen) and transiently transfected into COS-1 cells in six wells plates with lipofectamine (GIBCO BRL). After 48 hr, the cells were washed once with Hank's balanced salt solution (HBHA, Cheng and Flanagen, 1994), and then incubated in

HBHA containing 50-100 ng/ml SemaIII-AP fusion protein for 75 min at room temperature. Plates were washed in HBHA six times, fixed with acetone-formaldehyde, then washed twice in HBS as described by Cheng and Flanagen (1994). Plates were kept in a 65^{o}C incubator for 2 hr to inactivate the endogenous alkaline phosphatase activity in COS cells. The cells in the plates were stained for 2-6 hr in AP buffer containing the AP substrate BCIP and NBT (GIBCO BRL) as described previously by Cheng and Flanagan (1994). Staining of the cells was monitored using a dissecting microscope.

After identification of a positive pool, 10 ng of DNA from the pool was transfected into DH5α_competent cells and the transformants were subdivided into subpools of 200-300 colonies. These subpools were rescreened as described above, and a positive subpool subdivided further through two more rounds until a single positive plasmid (p28) was isolated. The insert DNA in the p28 plasmid was sequenced from both strands using a Licor (L4000) automated sequencer as well as by ^{33}P cycle sequencing.

Human cDNA library screening

A search of the human expressed sequence tag (EST) databases with the sequence of rat SR1 (p28) revealed many short sequences with homology to its middle portion . An EST clone (Genbank accession number R61632) was obtained from Genome System Inc. and used as a probe to screen a human fetal brain cDNA library (Stratagene) at high stingency, leading to the isolation of four overlapping cDNAs covering the full-length coding region of human SR1.

In situ hybridization

Cryosat sections (10 μm) were made from the brachial region of E14 rat embryos prefixed with 4% paraformaldehyde (PFA). In situ hybridization of these sections was performed as described by Schaeren-Wiemers and Gerfin-Moser (1993) and Kennedy et al (1994). A 1285 bp fragment including 490 bp of 5'-untranslated region and 795 bp of 5' SR1 coding region was released by Pst I digestion of the p28 plasmid and subcloned into pBluescript (Stratagene). Antisense and sense RNA probes were transcribed in the presence of digoxygenin-UTP (Boehringer Mannheim) using T7 and T3 polymerases as recommended by the manufacturer.

Cell surface binding and kinetic analysis

To examine the binding of SemaIII-AP to dissociated DRG cells, DRGs dissected from E14 or E18 rat embryos were digested with 0.25% of trypsin for 10 min at 37°C and

further dissociated by trituration with a fire-polished pipette. After removing the undissociated tissue clumps by precipitation, dissociated cells were collected by spinning at 430 x g for 5 min, then cultured in eight-well chamber slides at 37°C in 5% CO_2 for 20 hr in F12/N3 medium (Tessier-Lavigne et al., 1988) containing 0.5% fetal calf serum (FCS) and 25 ng/ml 2.5S NGF ((Bioproducts for Science Inc.). To examine binding activity, cells were incubated with HBHA buffer containing the indicated recombinant protein for 90 min, followed by washing, fixing, heating, and staining as described above.

293-EBNA cells stably expressing the full-length rat SR1 protein were established by transfection of a pCEP4-SR1 plasmid and selection with geneticin and hygromycin. The equilibrium-binding experiments were performed essentially as described (Flanagan and Leder, 1990; Cheng and Flanagan, 1994) using control 293-EBNA cells or SR1-expressing 293-EBNA cells cultured on six-well plates precoated with poly-D-lysine.

Generation of antibodies to SemaIII and SR1

For Western blotting studies on SemaIII, purified AP-S, a fusion of AP to the Sema domain of SemaIII, was used to raise a rabbit anti-serum. For function-blocking studies on SR1, a 1775 bp DNA fragment encoding amino acids 265 to 857 of SR1 was PCR amplified and subcloned into a bacterial expression vector pQE-9 (Qiagen) for the generation in E. Coli of a fusion protein comprising six histidine residues at its amino terminus. The His-tagged SR1 was expressed in XL1-Blue cells and purified according to manufacturer's instructions, and used to raise a rabbit anti-SR1 antiserum. Immunoglobulins in the anti-SR1 or preimmune sera were purified on protein A-Agarose (GIBCO BRL) columns. After application of the sera to the columns, the columns were washed first with 15 bed-volumns of 100 mM Tris (pH 8.0) and then with another 20 bed-volumns of 10 mM Tris (pH 8.0), then eluted with 5 bed volumns of 50 mM glycine (pH 3.0). The eluates from the columns were immediately neutralized by addition of 1/10 volume of 1 M Tris (pH 8.0), followed by concentration on a Centricon-10 device (Amicon). To deplete anti-SR1 antibodies from the antiserum, an equal volume of nickle-agarose beads was incubated with (or, for control, without) purified His-SR1 protein (1 mg/ml) at 4°C for 4 hr. After washing three times with F12 medium, the beads were incubated at 4°C for 3 hr with an equal volume of anti-SR1 serum. The supernatants were collected and then subjected to protein A-agarose affinity purification as described above.

Immunoprecipitation and Western analysis

To detect AP or AP fusion proteins by Western blotting, aliquots of the concentrated conditioned media were resolved by SDS-PAGE (8% gel). After transfer to nitrocellulose (Amersham), the proteins were probed with rabbit anti-AP antibody (DAKO). The blot was developed with BCIP and NBT as the substrate.

To detect an interaction between SR1 and SemaIII, 100 µl protein A-agarose beads (GIBCO BRL) were first incubated with 5 µg of anti-AP monoclonal antibody (Medix Biotech) in IP buffer (20 mM Hepes, pH 7.0, 100 mM NaCl, 1 mM EDTA, 1 mM DTT, and 0.02% NP-40) at 4°C for 2 hr. After washing three times with 1 ml of IP buffer, half of the beads (50 µl) were incubated with 2 µg of Kit-AP (Flanagan and Leder, 1990) or SR1-AP protein (containing the entire SR1 ectodomain) at 4°C for another 2 hr. Beads conjugated with recombinant proteins were then washed three times with IP buffer, and resuspended into 40 µl IP buffer containing 2 µg of myc-tagged Sema III protein. After the mixtures were incubated at 4°C for 3 hr, the beads were washed six times with 1 ml IP buffer. The bound proteins were released by boiling the beads in 50 µl SDS-containing sample buffer and analyzed by SDS-PAGE (8% gel) and Western blotting with a monoclonal antibody (9E10) against a C-terminal Myc-epitope tag.

Immunohistochemistry

For immunostaining to detect the expression of SR1 in E14 rat spinal cord, cryostat sections (10 µm) from unfixed frozen embryos were collected and fixed with acetone for 5 min. The staining was performed with preimmune serum (1:500), or anti-SR1 serum (1:500) as the primary antibody and biotinylated goat anti-rabbit Ig (5 ng/ml, Biorad) as the secondary antibody. Diaminobenzidine (Sigma) was used as a chromogen, with signal enhancement by a Vectastain Elite ABC kit (Vector). For staining of cultured cells, E14 rat DRG were cultured as above for 20 hr, incubated with the anti-SR1 antiserum or preimmune serum (1/500 dilution) for 1 hr at room temperature, washed 3 times, fixed with methanol, and the bound antibody was visualized using a Cy3-conjugated secondary antibody (Jackson Immunological Laboratories).

Collapse assay

The collapse assay was performed essentially as described by Raper and Kapfhammer (1990) and Luo et al. (1993), with minor modifications. In brief, DRG explants were dissected from E14 rat embryos, and cultured at 37°C in 5% CO_2 for 16-

20 hr on six-well plates precoated with poly-D-lysine (Sigma) and laminin (Becton Dickinson Labware) in F12/N3 medium containing 0.5% FCS and 25 ng/ml 2.5 S NGF. Small volumes of concentrated conditioned medium containing AP, SemaIII-AP, or SemaIII-myc were gently added into the culture medium, and the cultures were kept at 37°C for 1 hr. The explants were fixed with 4% PFA in PBS containing 10% sucrose for 15 min, then incubated with PHTX (PBS / 1% heat-inactivated goat serum / 1% Triton X-100) for 15 min. The explants were then stained with 2 μg/ml Rhodamine-Phalloidin (Molecular Probes) for 30 min, washed, and mounted with Fluoromount G (Fisher). As a control, aliquots of L-a-lysophosphatidic acid (LPA, Sigma) were added into the cultures at a final concentration of 1 μM (Jalink et al., 1994) and the cultures were incubated at 37°C for 3 min prior to fixation and staining. To examine the effect of preimmune or anti-SR1 antisera, aliquots of each antiserum were added into the explant cultures, which were kept at 37°C for 30 min prior to the addition of SemaIII protein or LPA.

Repulsion assay

The repulsion assay was essentially as previously described (Messersmith et al., 1995). In brief, E14 rat DRG explants were dissected and embedded in collagen gels with control 293 EBNA cells or 293 EBNA cells expressing SemaIII-AP. The indicated amount of antibodies were included into the culture medium (F12/N3 medium containing 0.5% FCS and 25 ng/ml 2.5 S NGF). After incubation at 37°C for 40 hr, the explants were fixed with 4% PFA in PBS for 2 hr, and followed by immunostaining with a neurofilament-specific antibody (NF-M, 1:1500; Lee et al., 1987) and a horseradish peroxidase-conjugated secondary antibody (Boehringer-Mannheim; 1:250) as described (Kennedy et al., 1994; Messersmith et al., 1995). The quantification of neurite outgrowth was performed as described (Messersmith et al., 1995).

Identification of Neuropilin-2

The extracellular domain of neuropilin-1 is comprised of several predicted structural domains: two CUB motifs (domains a1 and a2), two domains of homology to coagulation factors V and VIII (domains b1 and b2) and a MAM domain (domain c) (Takagi et al., 1991; Kawakami et al., 1996) (Figure 1 and 2a). To determine whether neuropilin-1 is a member of a family of related molecules, we searched for relatives by reverse transcription-PCR (RT-PCR) using three sets of degenerate forward primers (5.1, 5.2 and 5.3) and three sets of degenerate reverse primers (3.1, 3.2, and 3.3). The primers

were designed based on the sequences conserved among domain a2 and other CUB domain proteins (primer set 5.1), domains b1 and/or b2 and coagulation factors V and VIII (primer sets 5.2, 5.3 and 3.1), domain c and other MAM domain proteins (primer set 3.2), or a sequence in the cytoplasmic domain that is highly conserved among neuropilin homologues from different species (primer set 3.3) (see Experimental Procedures). Sequences were amplified from whole E11 mouse embryo mRNA and adult mouse brain mRNA using all pairwise combinations of 5' and 3' primer sets (except 5.3 and 3.1). In all cases, products of the size expected for neuropilin-1 were amplified and subcloned. More than a dozen cDNAs for each pair of primer sets were sequenced, and in all cases mouse *neuropilin-1* sequences were recovered. In addition, several of the cDNAs obtained by RT-PCR using primer sets 5.2 (b1 domain, KEWIQVD) and 3.3 (cytoplasmic domain, ENYNFE) encoded overlapping sequences that were related but not identical to a portion of the *neuropilin-1* sequence. These sequences were extended in both the 5' and 3' directions using a combination of cDNA library screening and RACE (rapid amplification of cDNA ends) (see Experimental Procedures).

From these experiments, the full length sequence of a new neuropilin-1-related molecule was assembled (Figure 3), which has been named neuropilin-2. By screening the expressed sequence tag (EST) data bases, we were also able to assemble the sequences of several human ESTs to predict the sequence of human neuropilin-2, which shares high homology (90% identity) with that of mouse neuropilin-2. The overall structure predicted for neuropilin-2 is identical to that of neuropilin-1, with all the same functional domains (Figure 4A). At the amino acid level, the sequence of neuropilin-2 is 44% identical to that of neuropilin-1, in both mouse and human. The homology is distributed over the entire length of the proteins, with highest homology in the transmembrane domain.

In the course of these experiments (see Experimental Procedures), we also discovered evidence for the existence of alternative forms of neuropilin-2 which may arise by alternative splicing. First, an alternate form with a divergent carboxy terminus was identified, which we have named neuropilin-2(b0) (we will use the names neuropilin-2 and neuropilin-2(a0) interchangeably to refer to the original isoform). The sequence of neuropilin-2(b0) diverges from that of neuropilin-2(a0) at amino acid 809, between the MAM domain and the transmembrane domain of neuropilin-2(a0) (Figure 4C).

Neuropilin-2(b0) is predicted from hydrophobicity analysis to have a transmembrane domain, followed by a cytoplasmic domain of similar length to that in neuropilin-2(a0), but these two domains are highly divergent from those of neuropilin-2(a0), sharing only 10% identity. An expressed sequence tag (EST) encoding human sequences (346bp fragment) corresponding to a portion of this diverged sequence was also found in the dbEST database (AA25840) (Figure 4C). To test the prediction that neuropilin-2(b0) is a transmembrane protein, we tagged this protein at its carboxyl terminus with a myc-epitope, expressed the tagged construct by transient transfection into COS 7 cells, and examined expression of the tagged protein using monoclonal antibody 9E10 directed against the epitope tag (Evan et al., 1985). Detection of the myc-tag at the carboxyl terminus of neuropilin-2(b0) by immunostaining required detergent permeabilization of the transfected cells, indicating that neuropilin-2 is indeed a transmembrane protein.

In addition, we found other isoforms of neuropilin-2(a0), including isoforms with insertions of 5, 17, or 22 (5+17) amino acids at amino acid 809 in neuropilin-2(a0), i.e. at the site of divergence of the a and b isoforms of neuropilin-2 (Figure 4B). The 22 amino acid insertion is the sum of the 5 and the 17 amino acid insertions (Figure 4B). We term these isoforms neuropilin-2(a5), neuropilin-2(a17) and neuropilin-2(a22). The isoform reported by Kolodkin et al. (1997) appears to be the rat neuropilin-2(a17) isoform. Similarly, we have found an isoform of neuropilin-2(b0) with the very same 5 amino acid insertion at amino acid 809, and which we name neuropilin-2(b5) (Figure 4B). The pattern of combinations of the 5 and 17 amino acid inserts that we have observed in different neuropilin-2 isoforms indicates that these different isoforms arise from splicing in of separate exons encoding the 5 and 17 amino acid stretches.

To determine whether the a and b isoforms of neuropilin-2 show different temporal patterns of expression, we performed RT-PCR using a 5' primer designed to a sequence shared between all neuropilin-2 isoforms, and two 3' primers unique to the sequences in the cytoplasmic domains of neuropilin-2(a) and of neuropilin-2(b) (see Experimental Procedures). Using E11 whole mouse embryo mRNA as a template we found that at E11 only an amplification product corresponding to neuropilin-2(a) could be detected. However, using adult mouse brain mRNA as a template, we detected amplification products corresponding to both neuropilin-2(a) and neuropilin-2(b). Taken together, these results indicate that different isoforms of neuropilin-2 might arise by

alternative splicing and that this splicing are regulated in a time-dependent or a cell type-dependent fashion.

Neuropilin-2 is expressed by specific classes of developing neurons. To determine whether neuropilin-2, like neuropilin, is a candidate for a receptor involved in axonal growth or guidance, we examined by in situ hybridization whether *neuropilin-2* mRNA is expressed by embyronic neurons during the period of axonal extension. Given the large number of isoforms of neuropilin-2 that appear to exist, we decided in this first survey to use a probe corresponding to sequences that extend from domain b2 through the cytoplasmic domain of neuropilin-2(a0) (see Experimental Procedures). Most of this probe corresponds to sequences that are shared between all isoforms.

Spinal cord. We first examined the pattern of expression of *neuropilin-2* in the region of the developing mouse spinal cord during the period of initial extension of axons of motor and sensory neurons (from E9.5), at the level of the forelimbs. This pattern was highly dynamic. *Neuropilin-2* mRNA was detected in the ventral spinal cord of E9.5 embryos, including the region of developing motorneurons. Expression was also strong in the floor plate and in tissue adjacent to the neural tube, including the somites and prospective dorsal root ganglia (DRGs) but not the notochord. Between E10.5 and E13.5 we compared the expression of *neuropilin-2* to that of *neuropilin-1*, which has already been described (Kawakami et al., 1996). By E10.5, the level of neuropilin-*2* expression had increased in the spinal cord. The whole ventral half of the spinal cord including the floor plate was heavily labeled, but expression was also strong in cells localized in the lateral margin of the dorsal aspect of the spinal cord, which may include commissural neuron cell bodies. *Neuropilin-1* expression was also detected in the ventral spinal cord but only in motorneurons, and was very weak or absent from the floor and roof plates. *Neuropilin-2* and *neuropilin-1* mRNAs were also coexpressed in prospective DRGS, although *neuropilin-2* expression was in addition high in non-neural tissues surrounding the spinal cord. A similar pattern of *neuropilin-2* expression was observed at E11.5. At E13.5, *neuropilin-2* expression had decreased and was now restricted to the ventral portion of the spinal cord. Both *neuropilins* were still expressed in motorneurons, but *neuropilin-2*-expressing cells were found througout in the entire ventral spinal cord whereas the expression pattern of *neuropilin-1* was more restricted. In addition, *neuropilin-1* was now strongly expressed in the dorsal spinal cord and in the DRGs,

whereas *neuropilin-2* expression in the DRGs was very weak, and only just above background level. Weak expression of *neuropilin-1* was also detected in the floor plate at this stage, but contrary to *neuropilin-2*, it was absent form the roof plate. Expression of *neuropilin-2* at E15.5 was unchanged in the spinal cord, though no expression was detectable in DRGs at this stage.

Sympathetic ganglia. As early as E11.5, *neuropilin-2* was detected in the ganglia of the sympathetic chain. This expression was more intense by E13.5, and had slightly decreased by E15.5). At this stage *neuropilin-2* mRNA could also be detected in neurons of the superior cervical ganglion. Expression was also observed in the region of the enteric nervous system.

Olfactory system. High level *neuropilin-2* expression was detected in all components of the olfactory system. Intense staining was observed at E13.5 and E15.5 in the vomeronasal organ, as well as in the accessory olfactory bulb, its target territory in the forebrain. *Neuropilin-1* is not expressed in the accessory olfactory system (Kawakami et al., 1996).

By E15.5, the olfactory epithelium strongly expressed *neuropilin-2*, but this expression was not homogenous, being higher rostrally. A high level of *neuropilin-2* mRNA was observed in the anterior olfactory nucleus and in the telencephalic regions interconnected to the olfactory bulb, such as the amygdala, the piriform cortex and the entorhinal cortex.

Neocortex. *Neuropilin-2* expression in the cortex was first detected around E13.5, and was restricted to the intermediate zone of the ventral and lateral regions of the cortex. The mesenchymal cells covering the cortex also showed high level expression of *neuropilin-2*. By E15.5 the staining was still confined to the intermediate zone, and was stronger in its lower portion. At birth, *neuropilin-2* expression was no longer detected in the cortex, with the exception of the cingulate cortex.

Hippocampal formation. The pattern of expression of *neuropilin-2* was particularly interesting in the components of the hippocampal formation. *Neuropilin-2* could be detected as early as E13.5 in the hippocampus, and by E15.5 expression was evident in both the dentate gyrus and in cells of CA3 and CA1 fields. The hybridization signal was uninterrupted and formed a continuum with *neuropilin-2* expressing cells in the intermediate zone of the neocortex. By P0, expression of *neuropilin-2* was still very

high in granule cells of the dentate gyrus, the hilus, and in the pyramidal cell layer, intermediate zone, and in the interneurons of the CA3-CA1 fields. Expression was also observed in the subiculum but not the presubiculum or the parasubiculum. At this stage, *neuropilin-2* expression was also very intense in most of the brain regions that project to the hippocampus. The neurons of the entorhinal cortex which project massively through the so-called perforant pathway to the dentate gyrus, the hippocampus and the subiculum, expressed *neuropilin-2*. Cells in the septal region (medial septum, diagonal band of Broca), another major source of afferent fibers to the hippocampal formation, also strongly expressed *neuropilin-2* at E15.5 and at birth.

Visual system. At E11.5, *neuropilin-2* was very highly expressed in the mesenchyme surrounding the eye-cup and the optic nerve, but was absent from the retina. At E15.5, low expression of *neuropilin-2* mRNA was detected in the ganglion cell layer, and diffuse expression was observed in the superior colliculus, one of the targets of retinal axons. By P0, *neuropilin-2* was very highly expressed in the most superficial layers of the superior colliculus, and at a lower level in the other layers. Expression stopped abruptly at the boundary between superior and inferior colliculus. Expression was not observed in the lateral geniculate nucleus of the thalamus at birth.

Thalamus. *Neuropilin-2* was also expressed at birth in several thalamic nuclei such as the medial habenula.

Cerebellum. *Neuropilin-2* expression was detected as early as E13.5 in the cerebellar primordium, and increased in level by E15.5. At P0, *neuropilin-2* was expressed in subsets of deep nuclei neurons as well as in stripes of Purkinje cells. *Neuropilin-1*, in contrast, is not expressed in the cerebellum (Kawakami et al., 1996).

Hindbrain nuclei. *Neuropilin-2* was detected at E15.5 and at birth (P0), in several branchiomotor nuclei, such as the trigeminal, facial and hypoglossal motor nuclei, but not in the dorsal motor nucleus of the vagus. We have not determined when expression in these nuclei starts. Lower levels of expression were observed in the regions of the inferior olive and vestibular nuclei. Expression was not detected in the pons, a region known to express *neuropilin-1* at high level (Kawakami et al., 1996).

Expression of *neuropilin-2* in non-neural tissues. In addition to its expression in the CNS, *neuropilin-2* was also detected in many non-neural tissues. At E10.5 it was expressed in the limb bud in restricted areas in the regions of the dorsal and ventral

muscle masses. Later on, expression was also observed in the developing bones, in particular in the vertebrae, ribs and digits. Expression of *neuropilin-2* was also observed in several muscles such as the back muscles and the tongue, and the strongest expression was observed in the region of the smooth muscles of the gut. Expression was also observed in the intestinal epithelium, as well as in cells in the kidney, the submandibular gland, the lung, the whisker follicles of the snout, and in the inner ear In contrast to *neuropilin-1* (Kawakami et al., 1996), *neuropilin-2* expression was not detected in the heart or in capillaries, but was found in the dorsal aorta.

Different binding patterns of neuropilin-1 and neuropilin-2 to different semaphorin family members. To test whether neuropilin-2, like neuropilin-1, is also a receptor for Sema III, we transiently expressed neuropilin-1, neuropilin-2(a0), -2(a5), -2(a22) and -2(b5) in COS-7 cells, for use in binding experiments. We were able to detect expression of neuropilin-1 and the different isoforms of neuropilin-2 in COS cells by immunostaining using either a polyclonal antibody against neuropilin-1 (He and Tessier-Lavigne, 1997) or monoclonal antibody 9E10 against the myc-tag at the carboxy terminus of all the neuropilin-2 isoforms. Western blot analysis showed that neuropilin-2 isoforms expressed in COS cells had the expected size of ~120kDa. To test for interactions with Sema III, we used a chimeric molecule in which Sema III was fused at its carboxy terminus to the histochemical reporter alkaline phosphatase (Sema III-AP: He and Tessier-Lavigne, 1997). Partially purified conditioned medium containing Sema III-AP was incubated with COS cells expressing neuropilins, and bound protein was detected by alkaline phosphatase histochemistry. As expected, Sema III-AP bound cells expressing neuropilin-1 (He and Tessier-Lavigne, 1997), and the alkaline phosphatase protein (AP) itself did not bind mock-transfected cells, cells expressing neuropilin-1, or any of the neuropilin-2 isoforms. Surprisingly, none of the isoforms of neuropilin-2 tested showed any detectable binding of Sema III-AP. We considered the possibility that neuropilin-2 binds the C terminal domain of Sema III and that the absence of binding was an artifact resulting from fusion of AP to the carboxy terminal portion of Sema III, masking the binding site. To address this possibility, we made use of a chimeric molecule in which AP is fused to the amino terminus of C domain of Sema III (AP-C: He and Tessier-Lavigne, 1997). The AP-C protein bound cells expressing neuropilin-1 but not cells expressing any of the neuropilin-2 isoforms. Thus, the absence of binding of full length

Sema III-AP to cells expressing the different neuropilin-2 isoforms reflects a bona fide absence of binding of Sema III to neuropilin-2.

Since Sema III itself does not appear to bind neuropilin-2, we wondered whether neuropilin-2 might be a receptor for other members of the semaphorin family. Sema III is a member of a subfamily of structurally-related molecules within the semaphorin family that includes the members Sema E/Collapsin-3 (Luo et al., 1995; Püschel et al., 1995), Sema IV/Sema 3F (Sekido et al., 1996; Roche et al., 1996; Xiang et al., 1996), Sema A/Sema V (Sekido et al., 1996), and Sema H. Like Sema III, all of these proteins are secreted proteins possessing a semaphorin domain, an immunoglubulin domain and a basic carboxy terminal domain (Püshel et al., 1995; Luo et al., 1995). We therefore examined whether two of these molecules, Sema E and Sema IV, are ligands for neuropilin-1 and/or neuropilin-2. In addition, we tested another secreted semaphorin, Drosophila Sema II (Kolodkin et al., 1993), which is more distantly related in sequence, as well as a more divergent semaphorin, the transmembrane Sema VIa (Zhou, et al 1997). As for Sema III, we tested the ability of COS cells expressing neuropilin-1 or neuropilin-2 to bind chimeric molecules in which alkaline phosphatase was fused to Sema E, Sema IV, Drosophila D-Sema II or the ectodomain of Sema VIa (see Experimental Procedures). These AP fusion proteins were presented to the cells in the form of partially purified conditioned media from cells expressing each of the proteins; media were matched for AP activity. We found that both neuropilin and different isoforms of neuropilin-2 expressing cells bound Sema E-AP and Sema IV-AP. In contrast, neither neuropilin-1 nor any of the neuropilin-2 isoforms expressed in COS cells showed detectable binding to the AP fusions with D-Sema II or the Sema VIa ectodomain. In control experiments, we found that Sema E-AP and Sema IV-AP did not bind mock-transfected COS cells or COS cells expressing the netrin-1 receptor DCC.

We estimated the binding affinity of the AP fusions of Sema III, Sema E and Sema IV to cells expressing neuropilin-1 or neuropilin-2 in equilibrium binding experiments. For these experiments, we used the a5 isoform of neuropilin-2. Specific binding curves of these molecules showed saturation and could be fitted with the Hill equation (Fig. 5A-5C). The estimated dissociation constants (Kd) for Sema E binding to neuropilin-1 and neuropilin-2 were 5 nM and 18 nM, respectively. Those for Sema IV binding to neuropilin-1 and neuropilin-2 were 30 nM and 5 nM, respectively. No

detectable binding of Sema III to neuropilin-2 expressing cells was detected, while the estimated Kd for Sema III binding to neuropilin-1 was 0.325 nM (see also He and Tessier-Lavigne, 1997). Similar Kd values were obtained using the b5 isoform of neuropilin-2 and the degree of binding of different semaphorins to cells all isoforms tested appeared similar.

Dynamic expression of *neuropilin-2* complementary to that of *neuropilin-1*. The specific pattern of expression of *neuropilin-2* indicates the involvement of members of the Sema III subfamily other than Sema III itself in the guidance of a variety of different axonal classes, in particular in the spinal cord, olfactory system, and hippocampus.

In the spinal cord, commissural axons are guided along a dorso-ventral trajectory at least partly in response to the diffusible chemoattractant netrin-1 (Serafini et al., 1996). *Neuropilin-2* transcripts are detected in the region of commissural neuron cell bodies, indicating that commissural neurons express *neuropilin-2*. Since *Sema E* is expressed in the ventral spinal cord (Püschel et al., 1995), this semaphorin might contribute to the guidance of commissural axons. Our in situ hybridization studies also indicate that different motorneuron populations express different complements of neuropilins, and therefore might respond differentially to different secreted semaphorins expressed in the periphery (Püschel et al., 1995; Wright et al., 1995; Giger et al., 1996). Thus, different semaphorins can contribute to patterning the projections of motor axons to distinct peripheral targets (Tsushida et al., 1994). The olfactory system is another site of significant *neuropilin-2* expression, suggesting a role for secreted semaphorins distinct from Sema III in guidance in this system. Axons from the olfactory bulb are known to be repelled by an unidentified septum-derived chemorepellent (Pini, 1993). *Neuropilin-2* transcripts are expressed in the region of the cell bodies of origin of these axons in the bulb, indicating that a secreted semaphorin can function as a septal-derived chemorepellent. Another interesting finding is that *neuropilin-2* expression in the olfactory epithelium (presumably by primary olfactory neurons) is not uniform, indicating that secreted semaphorins can play a role in differential guidance of different complements of primary olfactory axons, contributing to the creation of an olfactory map.

Neuropilins are also expressed in the sites of origin of afferent projections to the hippocampus. Afferents to the hippocampus are known to be topographically organized,

with septal, hippocampal, and entorhinal axons projecting to distinct dendritic locations on granule and pyramidal neurons (Paxinos 1995). *Neuropilin-1* and-*2* are expressed by the septal and hippocampal neurons, whereas only *neuropilin-2* is expressed by entorhinal neurons. *Sema E* and *Sema IV* are highly expressed in the hippocampus (Püschel et al., 1995; Sekido et al., 1996), and these semaphorins can therefore contribute to the patterning of hippocampal afferent projections as well.

Finally, the observation that *neuropilin-2* is expressed in many non-neuronal tissues also indicates the involvement of semaphorins other than Sema III in organogenesis outside the nervous system. A role for secreted semaphorins in tumor suppression is indicated by the fact that *neuropilin-2* is expressed in the lung, since *Sema IV* and *Sema A/V* map to a region of chromosome 3p that is frequently deleted in small cell lung cancer, and which is thought to contain a tumor suppressor gene for lung cancer (Roche et al., 1996; Sekido et al., 1996; Xiang et al., 1996).

Experimental Procedures: Isolation of neuropilin-2 and its splice variants

Six sets of fully degenerate oligonucleotides were used to perform RT-PCR using pfu polymerase (Stratagene) on mRNA isolated from E11 whole mouse embryo and adult mouse brain. Primers were designed to conserved amino acid sequences in the a2 domain of neuropilin, the b1 domain, the b2 domain , the MAM domain and the cytoplasmic domain. For each of the reactions, DNA bands of the size expected for neuropilin-1 were excised, and the gel purified DNA was subjected to secondary PCR amplification using the same primers but with an EcoR I site at the 5' terminus of forward primers and an Xba I site in the reverse primers. The PCR products were cloned into pBluescript KS(-) and sequenced. From one of these reactions, a novel sequence corresponding to neuropilin-2 was isolated (see Results). A 1.2kb fragment of *neuropilin-2* was used as a probe to screen an adult mouse brain gt11 lambda phage library (Clontech). Partial cDNA fragments isolated in this way corresponded to two presumptive differential splicing isoforms, the a and b forms, with or without the 5, 17 and 22 amino acid insertions (Figure 4). In order to obtain a full length cDNA, 5' RACE was performed on cDNA isolated from E11 mouse whole embryo and adult mouse brain. The 5'-RACE products were cloned into pBluescript KS(-) with 5' Not I and 3' Xho I sites, and sequenced. cDNAs containing the entire coding regions of the a and b isoforms of neuropilin-2 were assembled, with and without various combinations of the 5, 17 and 22 amino acid

insertions (see Results).

In situ hybridization. A 1200 nucleotide fragment of neuropilin-2 was used to generate digoxygenin (DIG)-labeled and ^{35}S-labeled antisense and sense RNA probes. In situ hybridization was performed on vibratome sections of P0 mouse brain with the DIG-labeled probe, and using the radioactive probe on cryosections taken at various stages between E9.5 and P0. The in situ hybridization procedures using digoxygenin-labeled probes were as described previously (Chédotal et al., 1996), and procedure using radioactive probes was as described by Messersmith et.al. (1995).

Plasmid construction. The coding regions of neuropilin-2 of alternative splicing forms, deleted of their signal sequences, were subcloned into the expression vector pSecTag-A (Invitrogen) in the Hind III (5'-end) and Xba I (3'-end) sites and transiently transfected into COS 7 cells using Lipofectamine (GIBCO BRL). Expression of neuropilin-2 isoforms was detected by immunocytochemistry and Western analysis using monoclonal antibody 9E10 (to the myc tag at the C terminus of the neuropilin-2 isoforms).

The semaphorin III-AP fusion protein was described previously (He and Tessier-Lavigne, 1997). The mouse Sema E clone was obtained by PCR from P0 mouse brain cDNAs, using the PCR primers. The amplified band was subcloned into the expression vector, APtag-4 vector which a sequence coding for secreted alkaline phosphatase. The human Sema IV clone was subcloned in pSecTag-A (Invitrogen), which also contains the secreted alkaline phosphatase.

Semaphorin-AP fusion protein binding assay. The semaphorin-AP fusion protein binding experiments was as described by Cheng and Flanagan (1994), with the exception that in order to reduce background binding, 2 μg/ml of heparin was included in the binding mixture. Briefly, neuropilin-1 and neuropilin-2 expression constructs were transiently expressed in COS 7 cells as described above. After 48 hours of transfection, expressing cells were rinsed with HBHA buffer (Hank's balanced salt solution with 20 mM HEPES pH 7.0, 0.05% sodium azide) (Cheng and Flanagan, 1994). Concentrated supernatant containing semaphorin-AP fusion proteins in the presence of 20 mM HEPES and 0.05 % of sodium azide was incubated with expressing COS cells at room temperature for 75 minutes, followed by heat inactivation of endogenous alkaline phosphatase, washing, and color development as described by Cheng and Flanagan

(1994).

Protocol for high throughput SR-SemaIII binding assay.

A. Reagents:

- Neutralite Avidin: 20 µg/ml in PBS.

- Blocking buffer: 5% BSA, 0.5% Tween 20 in PBS; 1 hour at room temperature.

- Assay Buffer: 100 mM KCl, 20 mM HEPES pH 7.6, 1 mM $MgCl_2$, 1% glycerol, 0.5% NP-40, 50 mM β-mercaptoethanol, 1 mg/ml BSA, cocktail of protease inhibitors.

- ^{33}P SR polypeptide 10x stock: 10^{-8} - 10^{-6} M "cold" SR polypeptide specific SR domain supplemented with 200,000-250,000 cpm of labeled SR (Beckman counter). Place in the 4°C microfridge during screening.

- Protease inhibitor cocktail (1000X): 10 mg Trypsin Inhibitor (BMB # 109894), 10 mg Aprotinin (BMB # 236624), 25 mg Benzamidine (Sigma # B-6506), 25 mg Leupeptin (BMB # 1017128), 10 mg APMSF (BMB # 917575), and 2mM $NaVO_3$ (Sigma # S-6508) in 10 ml of PBS.

-SemaIII: 10^{-7} - 10^{-5} M biotinylated SemaIII in PBS.

B. Preparation of assay plates:

- Coat with 120 µl of stock N-Avidin per well overnight at 4°C.

- Wash 2 times with 200 µl PBS.

- Block with 150 µl of blocking buffer.

- Wash 2 times with 200 µl PBS.

C. Assay:

- Add 40 µl assay buffer/well.

- Add 10 µl compound or extract.

- Add 10 µl ^{33}P-SR (20-25,000 cpm/0.1-10 pmoles/well =10^{-9}- 10^{-7} M final conc).

- Shake at 25°C for 15 minutes.

- Incubate additional 45 minutes at 25°C.

- Add 40 µM biotinylated SemaIII (0.1-10 pmoles/40 ul in assay buffer)

- Incubate 1 hour at room temperature.

- Stop the reaction by washing 4 times with 200 µM PBS.

- Add 150 µM scintillation cocktail.

- Count in Topcount.

D. Controls for all assays (located on each plate):

a. Non-specific binding

b. Soluble (non-biotinylated SemaIII) at 80% inhibition.

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All publications and patent applications cited in this specification are herein incorporated by reference as if each individual publication or patent application were specifically and individually indicated to be incorporated by reference. Although the foregoing invention has been described in some detail by way of illustration and example for purposes of clarity of understanding, it will be readily apparent to those of ordinary skill in the art in light of the teachings of this invention that certain changes and modifications may be made thereto without departing from the spirit or scope of the appended claims.

SEQUENCE LISTING

(1) GENERAL INFORMATION:
(i) APPLICANT: Tessier-Lavigne, Marc
He, Zhigang
Chen, Hang
(ii) TITLE OF INVENTION: Semaphorin Receptors
(iii) NUMBER OF SEQUENCES: 26
(iv) CORRESPONDENCE ADDRESS:
(A) ADDRESSEE: SCIENCE & TECHNOLOGY LAW GROUP
(B) STREET: 75 DENISE DRIVE
(C) CITY: HILLSBOROUGH
(D) STATE: CALIFORNIA
(E) COUNTRY: USA
(F) ZIP: 94010
(v) COMPUTER READABLE FORM:
(A) MEDIUM TYPE: Floppy disk
(B) COMPUTER: IBM PC compatible
(C) OPERATING SYSTEM: PC-DOS/MS-DOS
(D) SOFTWARE: PatentIn Release #1.0, Version #1.30
(vi) CURRENT APPLICATION DATA:
(A) APPLICATION NUMBER:
(B) FILING DATE:
(C) CLASSIFICATION:
(viii) ATTORNEY/AGENT INFORMATION:
(A) NAME: OSMAN, RICHARD A
(B) REGISTRATION NUMBER: 36,627
(C) REFERENCE/DOCKET NUMBER: UC97-288-2
(ix) TELECOMMUNICATION INFORMATION:
(A) TELEPHONE: (650) 343-4341
(B) TELEFAX: (650) 343-4342

human SP1

(2) INFORMATION FOR SEQ ID NO:1:
(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 2772 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: double
(D) TOPOLOGY: linear
(ii) MOLECULE TYPE: cDNA
(xi) SEQUENCE DESCRIPTION: SEQ ID NO:1:

ATGGAGAGGG GGCTGCCGCT CCTCTGCGCC GTGCTCGCCC TCGTCCTCGC CCCGGCCGGC 60
GCTTTTCGCA ACGATGAATG TGGCGATACT ATAAAAATTG AAAGCCCCGG GTACCTTACA 120
TCTCCTGGTT ATCCTCATTC TTATCACCCA AGTGAAAAAT GCGAATGGCT GATTCAGGCT 180
CCGGACCCAT ACCAGAGAAT TATGATCAAC TTCAACCCTC ACTTCGATTT GGAGGACAGA 240
GACTGCAAGT ATGACTACGT GGAAGTCTTC GATGGAGAAA ATGAAAATGG ACATTTTAGG 300
GGAAAGTTCT GTGGAAAGAT AGCCCCTCCT CCTGTTGTGT CTTCAGGGCC ATTTCTTTTT 360
ATCAAATTTG TCTCTGACTA CGAAACACAT GGTGCAGGAT TTTCCATACG TTATGAAATT 420
TTCAAGAGAG GTCCTGAATG TTCCCAGAAC TACACAACAC CTAGTGGAGT GATAAAGTCC 480
CCCGGATTCC CTGAAAAATA TCCCAACAGC CTTGAATGCA CTTATATTGT CTTTGCGCCA 540
AAGATGTCAG AGATTATCCT GGAATTTGAA AGCTTTGACC TGGAGCCTGA CTCAAATCCT 600
CCAGGGGGGA TGTTCTGTCG CTACGACCGG CTAGAAATCT GGGATGGATT CCCTGATGTT 660
GGCCCTCACA TTGGGCGTTA CTGTGGACAG AAAACACCAG GTCGAATCCG ATCCTCATCG 720
GGCATTCTCT CCATGGTTTT TTACACCGAC AGCGCGATAG CAAAAGAAGG TTTCTCAGCA 780
AACTACAGTG TCTTGCAGAG CAGTGTCTCA GAAGATTTCA AATGTATGGA AGCTCTGGGC 840
ATGGAATCAG GAGAAATTCA TTCTGACCAG ATCACAGCTT CTTCCCAGTA TAGCACCAAC 900
TGGTCTGCAG AGCGCTCCCG CCTGAACTAC CCTGAGAATG GGTGGACTCC CGGAGAGGAT 960
TCCTACCGAG AGTGGATACA GGTAGACTTG GGCCTTCTGC GCTTTGTCAC GGCTGTCGGG 1020
ACACAGGGCG CCATTTCAAA AGAAACCAAG AAGAAATATT ATGTCAAGAC TTACAAGATC 1080

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GACGTTAGCT CCAACGGGGA AGACTGGATC ACCATAAAAG AAGGAAACAA ACCTGTTCTC    1140
TTTCAGGGAA ACACCAACCC CACAGATGTT GTGGTTGCAG TATTCCCCAA ACCACTGATA    1200
ACTCGATTTG TCCGAATCAA GCCTGCAACT TGGGAAACTG GCATATCTAT GAGATTTGAA    1260
GTATACGGTT GCAAGATAAC AGATTATCCT TGCTCTGGAA TGTTGGGTAT GGTGTCTGGA    1320
CTTATTTCTG ACTCCCAGAT CACATCATCC AACCAAGGAG ACAGAAACTG GATGCCTGAA    1380
AACATCCGCC TGGTAACCAG TCGCTCTGGC TGGGCACTTC CACCCGCACC TCATTCCTAC    1440
ATCAATGAGT GGCTCCAAAT AGACCTGGGG GAGGAGAAGA TCGTGAGGGG CATCATCATT    1500
CAGGGTGGGA AGCACCGAGA GAACAAGGTG TTCATGAGGA AGTTCAAGAT CGGGTACAGC    1560
AACAACGGCT CGGACTGGAA GATGATCATG GATGACAGCA AACGCAAGGC GAAGTCTTTT    1620
GAGGGCAACA ACAACTATGA TACACCTGAG CTGCGGACTT TTCCAGCTCT CTCCACGCGA    1680
TTCATCAGGA TCTACCCCGA GAGAGCCACT CATGGCGGAC TGGGGCTCAG AATGGAGCTG    1740
CTGGGCTGTG AAGTGGAAGC CCCTACAGCT GGACCGACCA CTCCCAACGG GAACTTGGTG    1800
GATGAATGTG ATGACGACCA GGCCAACTGC CACAGTGGAA CAGGTGATGA CTTCCAGCTC    1860
ACAGGTGGCA CCACTGTGCT GGCCACAGAA AAGCCCACGG TCATAGACAG CACCATACAA    1920
TCAGAGTTTC CAACATATGG TTTTAACTGT GAATTTGGCT GGGGCTCTCA CAAGACCTTC    1980
TGCCACTGGG AACATGACAA TCACGTGCAG CTCAAGTGGA GTGTGTTGAC CAGCAAGACG    2040
GGACCCATTC AGGATCACAC AGGAGATGGC AACTTCATCT ATTCCCAAGC TGACGAAAAT    2100
CAGAAGGGCA AAGTGGCTCG CCTGGTGAGC CCTGTGGTTT ATTCCCAGAA CTCTGCCCAC    2160
TGCATGACCT TCTGGTATCA CATGTCTGGG TCCCACGTCG GCACACTCAG GGTCAAACTG    2220
CGCTACCAGA AGCCAGAGGA GTACGATCAG CTGGTCTGGA TGGCCATTGG ACACCAAGGT    2280
GACCACTGGA AGGAAGGGCG TGTCTTGCTC CACAAGTCTC TGAAACTTTA TCAGGTGATT    2340
TTCGAGGGCG AAATCGGAAA AGGAAACCTT GGTGGGATTG CTGTGGATGA CATTAGTATT    2400
AATAACCACA TTTCACAAGA AGATTGTGCA AAACCAGCAG ACCTGGATAA AAAGAACCCA    2460
GAAATTAAAA TTGATGAAAC AGGGAGCACG CCAGGATACG AAGGTGAAGG AGAAGGTGAC    2520
AAGAACATCT CCAGGAAGCC AGGCAATGTG TTGAAGACCT TAGAACCCAT CCTCATCACC    2580
ATCATAGCCA TGAGCGCCCT GGGGGTCCTC CTGGGGGCTG TCTGTGGGGT CGTGCTGTAC    2640
TGTGCCTGTT GGCATAATGG GATGTCAGAA AGAAACTTGT CTGCCCTGGA GAACTATAAC    2700
TTTGAACTTG TGGATGGTGT GAAGTTGAAA AAAGACAAAC TGAATACACA GAGTACTTAT    2760
TCGGAGGCAT GA                                                        2772
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(2) INFORMATION FOR SEQ ID NO:2:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 2588 amino acids

(B) TYPE: amino acid

(C) STRANDEDNESS: single

(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:2:

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Met Glu Thr Gly Leu Ala Arg Gly Gly Leu Tyr Leu Glu Pro Arg Leu
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Glu Leu Glu Cys Tyr Ser Ala Leu Ala Val Ala Leu Leu Glu Ala Leu
            20                  25                  30
Ala Leu Glu Val Ala Leu Leu Glu Ala Leu Ala Pro Arg Ala Leu Ala
        35                  40                  45
Gly Leu Tyr Ala Leu Ala Pro His Glu Ala Arg Gly Ala Ser Asn Ala
    50                  55                  60
Ser Pro Gly Leu Cys Tyr Ser Gly Leu Tyr Ala Ser Pro Thr His Arg
65                  70                  75                  80
Ile Leu Glu Leu Tyr Ser Ile Leu Glu Gly Leu Ser Glu Arg Pro Arg
                85                  90                  95
Gly Leu Tyr Thr Tyr Arg Leu Glu Thr His Arg Ser Glu Arg Pro Arg
            100                 105                 110
Gly Leu Tyr Thr Tyr Arg Pro Arg His Ile Ser Ser Glu Arg Thr Tyr
        115                 120                 125
Arg His Ile Ser Pro Arg Ser Glu Arg Gly Leu Leu Tyr Ser Cys Tyr
    130                 135                 140
Ser Gly Leu Thr Arg Pro Leu Glu Ile Leu Glu Gly Leu Asn Ala Leu
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145                 150                 155                 160
Ala Pro Arg Ala Ser Pro Pro Arg Thr Tyr Arg Gly Leu Asn Ala Arg
                165                 170                 175
Gly Ile Leu Glu Met Glu Thr Ile Leu Glu Ala Ser Asn Pro His Glu
            180                 185                 190
Ala Ser Asn Pro Arg His Ile Ser Pro His Glu Ala Ser Pro Leu Glu
        195                 200                 205
Gly Leu Ala Ser Pro Ala Arg Gly Ala Ser Pro Cys Tyr Ser Leu Tyr
    210                 215                 220
Ser Thr Tyr Arg Ala Ser Pro Thr Tyr Arg Val Ala Leu Gly Leu Val
225                 230                 235                 240
Ala Leu Pro His Glu Ala Ser Pro Gly Leu Tyr Gly Leu Ala Ser Asn
                245                 250                 255
Gly Leu Ala Ser Asn Gly Leu Tyr His Ile Ser Pro His Glu Ala Arg
            260                 265                 270
Gly Gly Leu Tyr Leu Tyr Ser Pro His Glu Cys Tyr Ser Gly Leu Tyr
        275                 280                 285
Leu Tyr Ser Ile Leu Glu Ala Leu Ala Pro Arg Pro Arg Pro Arg Val
    290                 295                 300
Ala Leu Val Ala Leu Ser Glu Arg Ser Glu Arg Gly Leu Tyr Pro Arg
305                 310                 315                 320
Pro His Glu Leu Glu Pro His Glu Ile Leu Glu Leu Tyr Ser Pro His
                325                 330                 335
Glu Val Ala Leu Ser Glu Arg Ala Ser Pro Thr Tyr Arg Gly Leu Thr
            340                 345                 350
His Arg His Ile Ser Gly Leu Tyr Ala Leu Ala Gly Leu Tyr Pro His
        355                 360                 365
Glu Ser Glu Arg Ile Leu Glu Ala Arg Gly Thr Tyr Arg Gly Leu Ile
    370                 375                 380
Leu Glu Pro His Glu Leu Tyr Ser Ala Arg Gly Gly Leu Tyr Pro Arg
385                 390                 395                 400
Gly Leu Cys Tyr Ser Ser Glu Arg Gly Leu Asn Ala Ser Asn Thr Tyr
                405                 410                 415
Arg Thr His Arg Thr His Arg Pro Arg Ser Glu Arg Gly Leu Tyr Val
            420                 425                 430
Ala Leu Ile Leu Glu Leu Tyr Ser Ser Glu Arg Pro Arg Gly Leu Tyr
        435                 440                 445
Pro His Glu Pro Arg Gly Leu Leu Tyr Ser Thr Tyr Arg Pro Arg Ala
    450                 455                 460
Ser Asn Ser Glu Arg Leu Glu Gly Leu Cys Tyr Ser Thr His Arg Thr
465                 470                 475                 480
Tyr Arg Ile Leu Glu Val Ala Leu Pro His Glu Ala Leu Ala Pro Arg
                485                 490                 495
Leu Tyr Ser Met Glu Thr Ser Glu Arg Gly Leu Ile Leu Glu Ile Leu
            500                 505                 510
Glu Leu Glu Gly Leu Pro His Glu Gly Leu Ser Glu Arg Pro His Glu
        515                 520                 525
Ala Ser Pro Leu Glu Gly Leu Pro Arg Ala Ser Pro Ser Glu Arg Ala
    530                 535                 540
Ser Asn Pro Arg Pro Arg Gly Leu Tyr Gly Leu Tyr Met Glu Thr Pro
545                 550                 555                 560
His Glu Cys Tyr Ser Ala Arg Gly Thr Tyr Arg Ala Ser Pro Ala Arg
                565                 570                 575
Gly Leu Glu Gly Leu Ile Leu Glu Thr Arg Pro Ala Ser Pro Gly Leu
            580                 585                 590
Tyr Pro His Glu Pro Arg Ala Ser Pro Val Ala Leu Gly Leu Tyr Pro
        595                 600                 605
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Arg His Ile Ser Ile Leu Glu Gly Leu Tyr Ala Arg Gly Thr Tyr Arg
    610                 615                 620
Cys Tyr Ser Gly Leu Tyr Gly Leu Asn Leu Tyr Ser Thr His Arg Pro
625                 630                 635                 640
Arg Gly Leu Tyr Ala Arg Gly Ile Leu Glu Ala Arg Gly Ser Glu Arg
                645                 650                 655
Ser Glu Arg Ser Glu Arg Gly Leu Tyr Ile Leu Glu Leu Glu Ser Glu
            660                 665                 670
Arg Met Glu Thr Val Ala Leu Pro His Glu Thr Tyr Arg Thr His Arg
        675                 680                 685
Ala Ser Pro Ser Glu Arg Ala Leu Ala Ile Leu Glu Ala Leu Ala Leu
    690                 695                 700
Tyr Ser Gly Leu Gly Leu Tyr Pro His Glu Ser Glu Arg Ala Leu Ala
705                 710                 715                 720
Ala Ser Asn Thr Tyr Arg Ser Glu Arg Val Ala Leu Leu Glu Gly Leu
                725                 730                 735
Asn Ser Glu Arg Ser Glu Arg Val Ala Leu Ser Glu Arg Gly Leu Ala
            740                 745                 750
Ser Pro Pro His Glu Leu Tyr Ser Cys Tyr Ser Met Glu Thr Gly Leu
        755                 760                 765
Ala Leu Ala Leu Glu Gly Leu Tyr Met Glu Thr Gly Leu Ser Glu Arg
    770                 775                 780
Gly Leu Tyr Gly Leu Ile Leu Glu His Ile Ser Ser Glu Arg Ala Ser
785                 790                 795                 800
Pro Gly Leu Asn Ile Leu Glu Thr His Arg Ala Leu Ala Ser Glu Arg
                805                 810                 815
Ser Glu Arg Gly Leu Asn Thr Tyr Arg Ser Glu Arg Thr His Arg Ala
            820                 825                 830
Ser Asn Thr Arg Pro Ser Glu Arg Ala Leu Ala Gly Leu Ala Arg Gly
        835                 840                 845
Ser Glu Arg Ala Arg Gly Leu Glu Ala Ser Asn Thr Tyr Arg Pro Arg
    850                 855                 860
Gly Leu Ala Ser Asn Gly Leu Tyr Thr Arg Pro Thr His Arg Pro Arg
865                 870                 875                 880
Gly Leu Tyr Gly Leu Ala Ser Pro Ser Glu Arg Thr Tyr Arg Ala Arg
                885                 890                 895
Gly Gly Leu Thr Arg Pro Ile Leu Glu Gly Leu Asn Val Ala Leu Ala
            900                 905                 910
Ser Pro Leu Glu Gly Leu Tyr Leu Glu Leu Glu Ala Arg Gly Pro His
        915                 920                 925
Glu Val Ala Leu Thr His Arg Ala Leu Ala Val Ala Leu Gly Leu Tyr
    930                 935                 940
Thr His Arg Gly Leu Asn Gly Leu Tyr Ala Leu Ala Ile Leu Glu Ser
945                 950                 955                 960
Glu Arg Leu Tyr Ser Gly Leu Thr His Arg Leu Tyr Ser Leu Tyr Ser
                965                 970                 975
Leu Tyr Ser Thr Tyr Arg Thr Tyr Arg Val Ala Leu Leu Tyr Ser Thr
            980                 985                 990
His Arg Thr Tyr Arg Leu Tyr Ser Ile Leu Glu Ala Ser Pro Val Ala
        995                 1000                1005
Leu Ser Glu Arg Ser Glu Arg Ala Ser Asn Gly Leu Tyr Gly Leu Ala
    1010                1015                1020
Ser Pro Thr Arg Pro Ile Leu Glu Thr His Arg Ile Leu Glu Leu Tyr
1025                1030                1035                1040
Ser Gly Leu Gly Leu Tyr Ala Ser Asn Leu Tyr Ser Pro Arg Val Ala
                1045                1050                1055
Leu Leu Glu Pro His Glu Gly Leu Asn Gly Leu Tyr Ala Ser Asn Thr
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            1060                1065                1070
His Arg Ala Ser Asn Pro Arg Thr His Arg Ala Ser Pro Val Ala Leu
        1075                1080                1085
Val Ala Leu Val Ala Leu Ala Leu Ala Val Ala Leu Pro His Glu Pro
    1090                1095                1100
Arg Leu Tyr Ser Pro Arg Leu Glu Ile Leu Glu Thr His Arg Ala Arg
1105                1110                1115                1120
Gly Pro His Glu Val Ala Leu Ala Arg Gly Ile Leu Glu Leu Tyr Ser
                1125                1130                1135
Pro Arg Ala Leu Ala Thr His Arg Thr Arg Pro Gly Leu Thr His Arg
            1140                1145                1150
Gly Leu Tyr Ile Leu Glu Ser Glu Arg Met Glu Thr Ala Arg Gly Pro
        1155                1160                1165
His Glu Gly Leu Val Ala Leu Thr Tyr Arg Gly Leu Tyr Cys Tyr Ser
    1170                1175                1180
Leu Tyr Ser Ile Leu Glu Thr His Arg Ala Ser Pro Thr Tyr Arg Pro
1185                1190                1195                1200
Arg Cys Tyr Ser Ser Glu Arg Gly Leu Tyr Met Glu Thr Leu Glu Gly
                1205                1210                1215
Leu Tyr Met Glu Thr Val Ala Leu Ser Glu Arg Gly Leu Tyr Leu Glu
            1220                1225                1230
Ile Leu Glu Ser Glu Arg Ala Ser Pro Ser Glu Arg Gly Leu Asn Ile
        1235                1240                1245
Leu Glu Thr His Arg Ser Glu Arg Ser Glu Arg Ala Ser Asn Gly Leu
    1250                1255                1260
Asn Gly Leu Tyr Ala Ser Pro Ala Arg Gly Ala Ser Asn Thr Arg Pro
1265                1270                1275                1280
Met Glu Thr Pro Arg Gly Leu Ala Ser Asn Ile Leu Glu Ala Arg Gly
                1285                1290                1295
Leu Glu Val Ala Leu Thr His Arg Ser Glu Arg Ala Arg Gly Ser Glu
            1300                1305                1310
Arg Gly Leu Tyr Thr Arg Pro Ala Leu Ala Leu Glu Pro Arg Pro Arg
        1315                1320                1325
Ala Leu Ala Pro Arg His Ile Ser Ser Glu Arg Thr Tyr Arg Ile Leu
    1330                1335                1340
Glu Ala Ser Asn Gly Leu Thr Arg Pro Leu Glu Gly Leu Asn Ile Leu
1345                1350                1355                1360
Glu Ala Ser Pro Leu Glu Gly Leu Tyr Gly Leu Gly Leu Leu Tyr Ser
                1365                1370                1375
Ile Leu Glu Val Ala Leu Ala Arg Gly Gly Leu Tyr Ile Leu Glu Ile
            1380                1385                1390
Leu Glu Ile Leu Glu Gly Leu Asn Gly Leu Tyr Gly Leu Tyr Leu Tyr
        1395                1400                1405
Ser His Ile Ser Ala Arg Gly Gly Leu Ala Ser Asn Leu Tyr Ser Val
    1410                1415                1420
Ala Leu Pro His Glu Met Glu Thr Ala Arg Gly Leu Tyr Ser Pro His
1425                1430                1435                1440
Glu Leu Tyr Ser Ile Leu Glu Gly Leu Tyr Thr Tyr Arg Ser Glu Arg
                1445                1450                1455
Ala Ser Asn Ala Ser Asn Gly Leu Tyr Ser Glu Arg Ala Ser Pro Thr
            1460                1465                1470
Arg Pro Leu Tyr Ser Met Glu Thr Ile Leu Glu Met Glu Thr Ala Ser
        1475                1480                1485
Pro Ala Ser Pro Ser Glu Arg Leu Tyr Ser Ala Arg Gly Leu Tyr Ser
    1490                1495                1500
Ala Leu Ala Leu Tyr Ser Ser Glu Arg Pro His Glu Gly Leu Gly Leu
1505                1510                1515                1520
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Tyr Ala Ser Asn Ala Ser Asn Ala Ser Asn Thr Tyr Arg Ala Ser Pro
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Thr His Arg Pro Arg Gly Leu Leu Glu Ala Arg Gly Thr His Arg Pro
1540 1545 1550
His Glu Pro Arg Ala Leu Ala Leu Glu Ser Glu Arg Thr His Arg Ala
1555 1560 1565
Arg Gly Pro His Glu Ile Leu Glu Ala Arg Gly Ile Leu Glu Thr Tyr
1570 1575 1580
Arg Pro Arg Gly Leu Ala Arg Gly Ala Leu Ala Thr His Arg His Ile
1585 1590 1595 1600
Ser Gly Leu Tyr Gly Leu Tyr Leu Glu Gly Leu Tyr Leu Glu Ala Arg
1605 1610 1615
Gly Met Glu Thr Gly Leu Leu Glu Leu Glu Gly Leu Tyr Cys Tyr Ser
1620 1625 1630
Gly Leu Val Ala Leu Gly Leu Ala Leu Ala Pro Arg Thr His Arg Ala
1635 1640 1645
Leu Ala Gly Leu Tyr Pro Arg Thr His Arg Thr His Arg Pro Arg Ala
1650 1655 1660
Ser Asn Gly Leu Tyr Ala Ser Asn Leu Glu Val Ala Leu Ala Ser Pro
1665 1670 1675 1680
Gly Leu Cys Tyr Ser Ala Ser Pro Ala Ser Pro Ala Ser Pro Gly Leu
1685 1690 1695
Asn Ala Leu Ala Ala Ser Asn Cys Tyr Ser His Ile Ser Ser Glu Arg
1700 1705 1710
Gly Leu Tyr Thr His Arg Gly Leu Tyr Ala Ser Pro Ala Ser Pro Pro
1715 1720 1725
His Glu Gly Leu Asn Leu Glu Thr His Arg Gly Leu Tyr Gly Leu Tyr
1730 1735 1740
Thr His Arg Thr His Arg Val Ala Leu Leu Glu Ala Leu Ala Thr His
1745 1750 1755 1760
Arg Gly Leu Leu Tyr Ser Pro Arg Thr His Arg Val Ala Leu Ile Leu
1765 1770 1775
Glu Ala Ser Pro Ser Glu Arg Thr His Arg Ile Leu Glu Gly Leu Asn
1780 1785 1790
Ser Glu Arg Gly Leu Pro His Glu Pro Arg Thr His Arg Thr Tyr Arg
1795 1800 1805
Gly Leu Tyr Pro His Glu Ala Ser Asn Cys Tyr Ser Gly Leu Pro His
1810 1815 1820
Glu Gly Leu Tyr Thr Arg Pro Gly Leu Tyr Ser Glu Arg His Ile Ser
1825 1830 1835 1840
Leu Tyr Ser Thr His Arg Pro His Glu Cys Tyr Ser His Ile Ser Thr
1845 1850 1855
Arg Pro Gly Leu His Ile Ser Ala Ser Pro Ala Ser Asn His Ile Ser
1860 1865 1870
Val Ala Leu Gly Leu Asn Leu Glu Leu Tyr Ser Thr Arg Pro Ser Glu
1875 1880 1885
Arg Val Ala Leu Leu Glu Thr His Arg Ser Glu Arg Leu Tyr Ser Thr
1890 1895 1900
His Arg Gly Leu Tyr Pro Arg Ile Leu Glu Gly Leu Asn Ala Ser Pro
1905 1910 1915 1920
His Ile Ser Thr His Arg Gly Leu Tyr Ala Ser Pro Gly Leu Tyr Ala
1925 1930 1935
Ser Asn Pro His Glu Ile Leu Glu Thr Tyr Arg Ser Glu Arg Gly Leu
1940 1945 1950
Asn Ala Leu Ala Ala Ser Pro Gly Leu Ala Ser Asn Gly Leu Asn Leu
1955 1960 1965
Tyr Ser Gly Leu Tyr Leu Tyr Ser Val Ala Leu Ala Leu Ala Ala Arg

```
    1970                1975                1980
Gly Leu Glu Val Ala Leu Ser Glu Arg Pro Arg Val Ala Leu Val Ala
1985                1990                1995                2000
Leu Thr Tyr Arg Ser Glu Arg Gly Leu Asn Ala Ser Asn Ser Glu Arg
                2005                2010                2015
Ala Leu Ala His Ile Ser Cys Tyr Ser Met Glu Thr Thr His Arg Pro
            2020                2025                2030
His Glu Thr Arg Pro Thr Tyr Arg His Ile Ser Met Glu Thr Ser Glu
        2035                2040                2045
Arg Gly Leu Tyr Ser Glu Arg His Ile Ser Val Ala Leu Gly Leu Tyr
    2050                2055                2060
Thr His Arg Leu Glu Ala Arg Gly Val Ala Leu Leu Tyr Ser Leu Glu
2065                2070                2075                2080
Ala Arg Gly Thr Tyr Arg Gly Leu Asn Leu Tyr Ser Pro Arg Gly Leu
                2085                2090                2095
Gly Leu Thr Tyr Arg Ala Ser Pro Gly Leu Asn Leu Glu Val Ala Leu
            2100                2105                2110
Thr Arg Pro Met Glu Thr Ala Leu Ala Ile Leu Glu Gly Leu Tyr His
        2115                2120                2125
Ile Ser Gly Leu Asn Gly Leu Tyr Ala Ser Pro His Ile Ser Thr Arg
    2130                2135                2140
Pro Leu Tyr Ser Gly Leu Gly Leu Tyr Ala Arg Gly Val Ala Leu Leu
2145                2150                2155                2160
Glu Leu Glu His Ile Ser Leu Tyr Ser Ser Glu Arg Leu Glu Leu Tyr
                2165                2170                2175
Ser Leu Glu Thr Tyr Arg Gly Leu Asn Val Ala Leu Ile Leu Glu Pro
            2180                2185                2190
His Glu Gly Leu Gly Leu Tyr Gly Leu Ile Leu Glu Gly Leu Tyr Leu
        2195                2200                2205
Tyr Ser Gly Leu Tyr Ala Ser Asn Leu Glu Gly Leu Tyr Gly Leu Tyr
    2210                2215                2220
Ile Leu Glu Ala Leu Ala Val Ala Leu Ala Ser Pro Ala Ser Pro Ile
2225                2230                2235                2240
Leu Glu Ser Glu Arg Ile Leu Glu Ala Ser Asn Ala Ser Asn His Ile
                2245                2250                2255
Ser Ile Leu Glu Ser Glu Arg Gly Leu Asn Gly Leu Ala Ser Pro Cys
            2260                2265                2270
Tyr Ser Ala Leu Ala Leu Tyr Ser Pro Arg Ala Leu Ala Ala Ser Pro
        2275                2280                2285
Leu Glu Ala Ser Pro Leu Tyr Ser Leu Tyr Ser Ala Ser Asn Pro Arg
    2290                2295                2300
Gly Leu Ile Leu Glu Leu Tyr Ser Ile Leu Glu Ala Ser Pro Gly Leu
2305                2310                2315                2320
Thr His Arg Gly Leu Tyr Ser Glu Arg Thr His Arg Pro Arg Gly Leu
                2325                2330                2335
Tyr Thr Tyr Arg Gly Leu Gly Leu Tyr Gly Leu Gly Leu Tyr Gly Leu
            2340                2345                2350
Gly Leu Tyr Ala Ser Pro Leu Tyr Ser Ala Ser Asn Ile Leu Glu Ser
        2355                2360                2365
Glu Arg Ala Arg Gly Leu Tyr Ser Pro Arg Gly Leu Tyr Ala Ser Asn
    2370                2375                2380
Val Ala Leu Leu Glu Leu Tyr Ser Thr His Arg Leu Glu Gly Leu Pro
2385                2390                2395                2400
Arg Ile Leu Glu Leu Glu Ile Leu Glu Thr His Arg Ile Leu Glu Ile
                2405                2410                2415
Leu Glu Ala Leu Ala Met Glu Thr Ser Glu Arg Ala Leu Ala Leu Glu
            2420                2425                2430
```

```
Gly Leu Tyr Val Ala Leu Leu Glu Leu Glu Gly Leu Tyr Ala Leu Ala
        2435                2440                2445
Val Ala Leu Cys Tyr Ser Gly Leu Tyr Val Ala Leu Val Ala Leu Leu
    2450                2455                2460
Glu Thr Tyr Arg Cys Tyr Ser Ala Leu Ala Cys Tyr Ser Thr Arg Pro
2465                2470                2475                2480
His Ile Ser Ala Ser Asn Gly Leu Tyr Met Glu Thr Ser Glu Arg Gly
                2485                2490                2495
Leu Ala Arg Gly Ala Ser Asn Leu Glu Ser Glu Arg Ala Leu Ala Leu
            2500                2505                2510
Glu Gly Leu Ala Ser Asn Thr Tyr Arg Ala Ser Asn Pro His Glu Gly
        2515                2520                2525
Leu Leu Glu Val Ala Leu Ala Ser Pro Gly Leu Tyr Val Ala Leu Leu
    2530                2535                2540
Tyr Ser Leu Glu Leu Tyr Ser Leu Tyr Ser Ala Ser Pro Leu Tyr Ser
2545                2550                2555                2560
Leu Glu Ala Ser Asn Thr His Arg Gly Leu Asn Ser Glu Arg Thr His
                2565                2570                2575
Arg Thr Tyr Arg Ser Glu Arg Gly Leu Ala Leu Ala
            2580                2585
```

(2) INFORMATION FOR SEQ ID NO:3:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 2766 base pairs

(B) TYPE: nucleic acid

(C) STRANDEDNESS: double

(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: cDNA

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:3:

```
ATGGAGAGGG GGCTGCCGTT GCTGTGCGCC ACGCTCGCCC TTGCCCTCGC CCTGGGGGCT      60
TTCCGCAGCG ATAAATGTGG CGGGACTATA AAAATTGAAA ACCCGGGGTA CCTTACATCT     120
CCCGGCTACC CTCATTCTTA CCATCCAAGT GAGAAATGTG AATGGCTAAT CCAAGCTCCG     180
GAGCCCTACC AGAGAATCAT GATCAACTTC AACCCACATT TCGATTTGGA GGACAGAGAC     240
TGCAAGTATG ACTATGTGGA AGTGATCGAT GGAGAGAATG AAGGTGGCCG CCTGTGGGGG     300
AAGTTCTGTG GGAAGATCGC ACCTTCACCT GTGGTGTCTT CAGGGCCATT TCTCTTCATC     360
AAATTTGTCT CTGACTATGA GACCCACGGG GCAGGATTTT CCATCCGCTA TGAAATCTTC     420
AAGAGAGGGC CCGAATGTTC TCAGAACTAT ACAGCACCTA CTGGAGTGAT AAAGTCCCCT     480
GGGTTCCCTG AAAAATACCC CAACAGCTTG GAGTGCACCT ACATCATCTT TGCACCAAAG     540
ATGTCTGAGA TAATCCTAGA GTTTGAAAGT TTTGACCTGG AGCAAGACTC AAATCCTCCC     600
GGAGGAATGT TCTGTCGCTA TGACCGGCTG GAGATCTGGG ATGGATTCCC TGAAGTTGGC     660
CCTCACATTG GGCGTTACTG TGGGCAGAAA ACTCCTGGCC GGATCCGCTC CTCTTCAGGC     720
ATTCTATCCA TGGTCTTCTA CACTGACAGC GCAATAGCAA AGGAAGGTTT CTCAGCCAAC     780
TACAGCGTGC TGCAGAGCAG CATCTCTGAA GATTTCAAGT GTATGGAGGC TCTGGGCATG     840
GAATCTGGAG AGATCCATTC TGACCAGATC ACTGCATCTT CCCAGTATGG TACCAACTGG     900
TCTGTTGAGC GCTCCCGCCT GAACTACCCT GAAAACGGGT GGACACCAGG AGAGGACTCC     960
TACAGGGAGT GGATCCAGGT GGACTTGGGC CTCCTGCGAT TCGTTACTGC TGTGGGGACA    1020
CAGGGTGCCA TTTCCAAGGA AACCAAGAAG AAATATTATG TCAAGACTTA CAGAGTAGAC    1080
ATCAGCTCCA ACGGAGAGGA CTGGATCACC CTGAAGGAGG GAAATAAAGC CATTATCTTT    1140
CAGGGAAACA CCAATCCCAC GGATGTTGTC TTTGGAGTTT TCCCCAAACC ACTGATAACT    1200
CGATTTGTCC GAATCAAACC TGCATCCTGG GAAACTGGAA TATCTATGAG ATTTGAAGTT    1260
TATGGCTGCA AGATAACAGA TTACCCTTGC TCTGGAATGT TGGGCATGGT GTCTGGACTT    1320
ATTTCAGACT CCCAGATTAC AGCATCCAAC CAAGGAGACA GGAACTGGAT GCCAGAAAAC    1380
ATCCGCCTGG TGACCAGTCG AACCGGCTGG GCCCTGCCAC CCTCACCCCA CCCATACATC    1440
AATGAATGGC TCCAAGTGGA CCTGGGAGAT GAGAAGATAG TAAGAGGTGT CATCATTCAA    1500
GGTGGGAAGC ACCGAGAAAA CAAAGTGTTC ATGAGGAAGT TCAAGATCGC CTACAGTAAC    1560
AATGGTTCTG ACTGGAAAAT GATCATGGAT GACAGCAAGC GCAAGGCTAA GTCTTTTGAA    1620
GGCAACAACA ACTATGACAC ACCTGAGCTC CGGGCCTTTA CACCTCTCTC CACAAGATTC    1680
```

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ATCAGGATCT ACCCCGAGAG AGCCACACAT AGTGGGCTCG GACTGAGGAT GGAGCTACTG    1740
GGCTGTGAAG TAGAAGTGCC TACAGCTGGA CCCACGACAC CCAATGGGAA CCCCGTGGAC    1800
GAGTGTGACG ATGACCAGGC CAACTGCCAC AGTGGCACAG GTGATGACTT CCAGCTCACA    1860
GGAGGCACCA CTGTCCTGGC CACAGAGAAG CCCACCATTA TAGACAGCAC CATCCAATCA    1920
GAGTTCCCGA CATACGGTTT TAACTGCGAG TTTGGCTGGG GCTCTCACAA GACATTCTGC    1980
CACTGGGAAC ATGACAGCCA CGCGCAGCTC AGGTGGAGGG TGCTGACCAG CAAGACGGGG    2040
CCCATTCAGG ACCACACAGG AGATGGCAAC TTCATCTATT CCCAAGCTGA TGAAAATCAG    2100
AAAGGCAAAG TAGCCCGCCT GGTGAGCCCT GTGGTCTATT CCCAGAGTTC TGCCCACTGC    2160
ATGACCTTCT GGTATCACAT GTCCGGCTCT CATGTGGGTA CACTGAGGGT CAAACTGCAC    2220
TACCAGAAGC CAGAGGAATA TGATCAACTG GTCTGGATGG TGGTCGGGCA CCAAGGAGAC    2280
CACTGGAAGG AAGGGCGTGT CTTGCTGCAC AAATCTCTGA AACTGTATCA GGTTATTTTT    2340
GAAGGTGAAA TCGGAAAAGG AAACCTCGGT GGGATTGCTG TGGATGATAT CAGTATTAAC    2400
AACCACATTC CTCAGGAGGA CTGTGCAAAA CCAACAGACC TAGATAAAAA GAACACAGAA    2460
ATTAAAATAG ATGAAACAGG GAGCACCCCA GGATATGAAG AAGGGAAAGG CGACAAGAAC    2520
ATCTCCAGGA AGCCAGGCAA TGTGCTTAAG ACCCTGGACC CCATCCTGAT CACCATCATA    2580
GCCATGAGTG CCCTGGGGGT GCTCCTGGGT GCAGTCTGTG GAGTTGTGCT GTACTGTGCC    2640
TGTTGGCACA ATGGGATGTC GGAAAGGAAC CTATCTGCCC TGGAGAACTA TAACTTTGAA    2700
CTTGTGGATG GTGTAAAGTT GAAAAAAGAT AAACTGAACC CACACAGTAA TTACTCAGAG    2760
GCGTGA                                                               2766
```

(2) INFORMATION FOR SEQ ID NO:4:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 2584 amino acids

(B) TYPE: amino acid

(C) STRANDEDNESS: single

(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:4:

```
Met Glu Thr Gly Leu Ala Arg Gly Gly Leu Tyr Leu Glu Pro Arg Leu
1               5                  10                  15
Glu Leu Glu Cys Tyr Ser Ala Leu Ala Thr His Arg Leu Glu Ala Leu
            20                  25                  30
Ala Leu Glu Ala Leu Ala Leu Glu Ala Leu Ala Leu Glu Gly Leu Tyr
        35                  40                  45
Ala Leu Ala Pro His Glu Ala Arg Gly Ser Glu Arg Ala Ser Pro Leu
    50                  55                  60
Tyr Ser Cys Tyr Ser Gly Leu Tyr Gly Leu Tyr Thr His Arg Ile Leu
65                  70                  75                  80
Glu Leu Tyr Ser Ile Leu Glu Gly Leu Ala Ser Asn Pro Arg Gly Leu
                85                  90                  95
Tyr Thr Tyr Arg Leu Glu Thr His Arg Ser Glu Arg Pro Arg Gly Leu
            100                 105                 110
Tyr Thr Tyr Arg Pro Arg His Ile Ser Ser Glu Arg Thr Tyr Arg His
        115                 120                 125
Ile Ser Pro Arg Ser Glu Arg Gly Leu Leu Tyr Ser Cys Tyr Ser Gly
    130                 135                 140
Leu Thr Arg Pro Leu Glu Ile Leu Glu Gly Leu Asn Ala Leu Ala Pro
145                 150                 155                 160
Arg Gly Leu Pro Arg Thr Tyr Arg Gly Leu Asn Ala Arg Gly Ile Leu
                165                 170                 175
Glu Met Glu Thr Ile Leu Glu Ala Ser Asn Pro His Glu Ala Ser Asn
            180                 185                 190
Pro Arg His Ile Ser Pro His Glu Ala Ser Pro Leu Glu Gly Leu Ala
        195                 200                 205
Ser Pro Ala Arg Gly Ala Ser Pro Cys Tyr Ser Leu Tyr Ser Thr Tyr
    210                 215                 220
Arg Ala Ser Pro Thr Tyr Arg Val Ala Leu Gly Leu Val Ala Leu Ile
```

```
225                 230                 235                 240
Leu Glu Ala Ser Pro Gly Leu Tyr Gly Leu Ala Ser Asn Gly Leu Gly
                245                 250                 255
Leu Tyr Gly Leu Tyr Ala Arg Gly Leu Glu Thr Arg Pro Gly Leu Tyr
            260                 265                 270
Leu Tyr Ser Pro His Glu Cys Tyr Ser Gly Leu Tyr Leu Tyr Ser Ile
        275                 280                 285
Leu Glu Ala Leu Ala Pro Arg Ser Glu Arg Pro Arg Val Ala Leu Val
    290                 295                 300
Ala Leu Ser Glu Arg Ser Glu Arg Gly Leu Tyr Pro Arg Pro His Glu
305                 310                 315                 320
Leu Glu Pro His Glu Ile Leu Glu Leu Tyr Ser Pro His Glu Val Ala
                325                 330                 335
Leu Ser Glu Arg Ala Ser Pro Thr Tyr Arg Gly Leu Thr His Arg His
            340                 345                 350
Ile Ser Gly Leu Tyr Ala Leu Ala Gly Leu Tyr Pro His Glu Ser Glu
        355                 360                 365
Arg Ile Leu Glu Ala Arg Gly Thr Tyr Arg Gly Leu Ile Leu Glu Pro
    370                 375                 380
His Glu Leu Tyr Ser Ala Arg Gly Gly Leu Tyr Pro Arg Gly Leu Cys
385                 390                 395                 400
Tyr Ser Ser Glu Arg Gly Leu Asn Ala Ser Asn Thr Tyr Arg Thr His
                405                 410                 415
Arg Ala Leu Ala Pro Arg Thr His Arg Gly Leu Tyr Val Ala Leu Ile
            420                 425                 430
Leu Glu Leu Tyr Ser Ser Glu Arg Pro Arg Gly Leu Tyr Pro His Glu
        435                 440                 445
Pro Arg Gly Leu Leu Tyr Ser Thr Tyr Arg Pro Arg Ala Ser Asn Ser
    450                 455                 460
Glu Arg Leu Glu Gly Leu Cys Tyr Ser Thr His Arg Thr Tyr Arg Ile
465                 470                 475                 480
Leu Glu Ile Leu Glu Pro His Glu Ala Leu Ala Pro Arg Leu Tyr Ser
                485                 490                 495
Met Glu Thr Ser Glu Arg Gly Leu Ile Leu Glu Ile Leu Glu Leu Glu
            500                 505                 510
Gly Leu Pro His Glu Gly Leu Ser Glu Arg Pro His Glu Ala Ser Pro
        515                 520                 525
Leu Glu Gly Leu Gly Leu Asn Ala Ser Pro Ser Glu Arg Ala Ser Asn
    530                 535                 540
Pro Arg Pro Arg Gly Leu Tyr Gly Leu Tyr Met Glu Thr Pro His Glu
545                 550                 555                 560
Cys Tyr Ser Ala Arg Gly Thr Tyr Arg Ala Ser Pro Ala Arg Gly Leu
                565                 570                 575
Glu Gly Leu Ile Leu Glu Thr Arg Pro Ala Ser Pro Gly Leu Tyr Pro
            580                 585                 590
His Glu Pro Arg Gly Leu Val Ala Leu Gly Leu Tyr Pro Arg His Ile
        595                 600                 605
Ser Ile Leu Glu Gly Leu Tyr Ala Arg Gly Thr Tyr Arg Cys Tyr Ser
    610                 615                 620
Gly Leu Tyr Gly Leu Asn Leu Tyr Ser Thr His Arg Pro Arg Gly Leu
625                 630                 635                 640
Tyr Ala Arg Gly Ile Leu Glu Ala Arg Gly Ser Glu Arg Ser Glu Arg
                645                 650                 655
Ser Glu Arg Gly Leu Tyr Ile Leu Glu Leu Glu Ser Glu Arg Met Glu
            660                 665                 670
Thr Val Ala Leu Pro His Glu Thr Tyr Arg Thr His Arg Ala Ser Pro
        675                 680                 685
```

```
Ser Glu Arg Ala Leu Ala Ile Leu Glu Ala Leu Ala Leu Tyr Ser Gly
    690                 695                 700
Leu Gly Leu Tyr Pro His Glu Ser Glu Arg Ala Leu Ala Ala Ser Asn
705                 710                 715                 720
Thr Tyr Arg Ser Glu Arg Val Ala Leu Leu Glu Gly Leu Asn Ser Glu
                725                 730                 735
Arg Ser Glu Arg Ile Leu Glu Ser Glu Arg Gly Leu Ala Ser Pro Pro
            740                 745                 750
His Glu Leu Tyr Ser Cys Tyr Ser Met Glu Thr Gly Leu Ala Leu Ala
        755                 760                 765
Leu Glu Gly Leu Tyr Met Glu Thr Gly Leu Ser Glu Arg Gly Leu Tyr
    770                 775                 780
Gly Leu Ile Leu Glu His Ile Ser Ser Glu Arg Ala Ser Pro Gly Leu
785                 790                 795                 800
Asn Ile Leu Glu Thr His Arg Ala Leu Ala Ser Glu Arg Ser Glu Arg
                805                 810                 815
Gly Leu Asn Thr Tyr Arg Gly Leu Tyr Thr His Arg Ala Ser Asn Thr
            820                 825                 830
Arg Pro Ser Glu Arg Val Ala Leu Gly Leu Ala Arg Gly Ser Glu Arg
        835                 840                 845
Ala Arg Gly Leu Glu Ala Ser Asn Thr Tyr Arg Pro Arg Gly Leu Ala
    850                 855                 860
Ser Asn Gly Leu Tyr Thr Arg Pro Thr His Arg Pro Arg Gly Leu Tyr
865                 870                 875                 880
Gly Leu Ala Ser Pro Ser Glu Arg Thr Tyr Arg Ala Arg Gly Gly Leu
                885                 890                 895
Thr Arg Pro Ile Leu Glu Gly Leu Asn Val Ala Leu Ala Ser Pro Leu
            900                 905                 910
Glu Gly Leu Tyr Leu Glu Leu Glu Ala Arg Gly Pro His Glu Val Ala
        915                 920                 925
Leu Thr His Arg Ala Leu Ala Val Ala Leu Gly Leu Tyr Thr His Arg
    930                 935                 940
Gly Leu Asn Gly Leu Tyr Ala Leu Ala Ile Leu Glu Ser Glu Arg Leu
945                 950                 955                 960
Tyr Ser Gly Leu Thr His Arg Leu Tyr Ser Leu Tyr Ser Leu Tyr Ser
                965                 970                 975
Thr Tyr Arg Thr Tyr Arg Val Ala Leu Leu Tyr Ser Thr His Arg Thr
            980                 985                 990
Tyr Arg Ala Arg Gly Val Ala Leu Ala Ser Pro Ile Leu Glu Ser Glu
        995                 1000                1005
Arg Ser Glu Arg Ala Ser Asn Gly Leu Tyr Gly Leu Ala Ser Pro Thr
    1010                1015                1020
Arg Pro Ile Leu Glu Thr His Arg Leu Glu Leu Tyr Ser Gly Leu Gly
1025                1030                1035                1040
Leu Tyr Ala Ser Asn Leu Tyr Ser Ala Leu Ala Ile Leu Glu Ile Leu
                1045                1050                1055
Glu Pro His Glu Gly Leu Asn Gly Leu Tyr Ala Ser Asn Thr His Arg
            1060                1065                1070
Ala Ser Asn Pro Arg Thr His Arg Ala Ser Pro Val Ala Leu Val Ala
        1075                1080                1085
Leu Pro His Glu Gly Leu Tyr Val Ala Leu Pro His Glu Pro Arg Leu
    1090                1095                1100
Tyr Ser Pro Arg Leu Glu Ile Leu Glu Thr His Arg Ala Arg Gly Pro
1105                1110                1115                1120
His Glu Val Ala Leu Ala Arg Gly Ile Leu Glu Leu Tyr Ser Pro Arg
                1125                1130                1135
Ala Leu Ala Ser Glu Arg Thr Arg Pro Gly Leu Thr His Arg Gly Leu
```

```
            1140                1145                1150
Tyr Ile Leu Glu Ser Glu Arg Met Glu Thr Ala Arg Gly Pro His Glu
        1155                1160                1165
Gly Leu Val Ala Leu Thr Tyr Arg Gly Leu Tyr Cys Tyr Ser Leu Tyr
    1170                1175                1180
Ser Ile Leu Glu Thr His Arg Ala Ser Pro Thr Tyr Arg Pro Arg Cys
1185                1190                1195                1200
Tyr Ser Ser Glu Arg Gly Leu Tyr Met Glu Thr Leu Glu Gly Leu Tyr
                1205                1210                1215
Met Glu Thr Val Ala Leu Ser Glu Arg Gly Leu Tyr Leu Glu Ile Leu
            1220                1225                1230
Glu Ser Glu Arg Ala Ser Pro Ser Glu Arg Gly Leu Asn Ile Leu Glu
        1235                1240                1245
Thr His Arg Ala Leu Ala Ser Glu Arg Ala Ser Asn Gly Leu Asn Gly
    1250                1255                1260
Leu Tyr Ala Ser Pro Ala Arg Gly Ala Ser Asn Thr Arg Pro Met Glu
1265                1270                1275                1280
Thr Pro Arg Gly Leu Ala Ser Asn Ile Leu Glu Ala Arg Gly Leu Glu
                1285                1290                1295
Val Ala Leu Thr His Arg Ser Glu Arg Ala Arg Gly Thr His Arg Gly
            1300                1305                1310
Leu Tyr Thr Arg Pro Ala Leu Ala Leu Glu Pro Arg Pro Arg Ser Glu
        1315                1320                1325
Arg Pro Arg His Ile Ser Pro Arg Thr Tyr Arg Ile Leu Glu Ala Ser
    1330                1335                1340
Asn Gly Leu Thr Arg Pro Leu Glu Gly Leu Asn Val Ala Leu Ala Ser
1345                1350                1355                1360
Pro Leu Glu Gly Leu Tyr Ala Ser Pro Gly Leu Leu Tyr Ser Ile Leu
                1365                1370                1375
Glu Val Ala Leu Ala Arg Gly Gly Leu Tyr Val Ala Leu Ile Leu Glu
            1380                1385                1390
Ile Leu Glu Gly Leu Asn Gly Leu Tyr Gly Leu Tyr Leu Tyr Ser His
        1395                1400                1405
Ile Ser Ala Arg Gly Gly Leu Ala Ser Asn Leu Tyr Ser Val Ala Leu
    1410                1415                1420
Pro His Glu Met Glu Thr Ala Arg Gly Leu Tyr Ser Pro His Glu Leu
1425                1430                1435                1440
Tyr Ser Ile Leu Glu Ala Leu Ala Thr Tyr Arg Ser Glu Arg Ala Ser
                1445                1450                1455
Asn Ala Ser Asn Gly Leu Tyr Ser Glu Arg Ala Ser Pro Thr Arg Pro
            1460                1465                1470
Leu Tyr Ser Met Glu Thr Ile Leu Glu Met Glu Thr Ala Ser Pro Ala
        1475                1480                1485
Ser Pro Ser Glu Arg Leu Tyr Ser Ala Arg Gly Leu Tyr Ser Ala Leu
    1490                1495                1500
Ala Leu Tyr Ser Ser Glu Arg Pro His Glu Gly Leu Gly Leu Tyr Ala
1505                1510                1515                1520
Ser Asn Ala Ser Asn Ala Ser Asn Thr Tyr Arg Ala Ser Pro Thr His
                1525                1530                1535
Arg Pro Arg Gly Leu Leu Glu Ala Arg Gly Ala Leu Ala Pro His Glu
            1540                1545                1550
Thr His Arg Pro Arg Leu Glu Ser Glu Arg Thr His Arg Ala Arg Gly
        1555                1560                1565
Pro His Glu Ile Leu Glu Ala Arg Gly Ile Leu Glu Thr Tyr Arg Pro
    1570                1575                1580
Arg Gly Leu Ala Arg Gly Ala Leu Ala Thr His Arg His Ile Ser Ser
1585                1590                1595                1600
```

Glu Arg Gly Leu Tyr Leu Glu Gly Leu Tyr Leu Glu Ala Arg Gly Met
1605 1610 1615
Glu Thr Gly Leu Leu Glu Leu Glu Gly Leu Tyr Cys Tyr Ser Gly Leu
1620 1625 1630
Val Ala Leu Gly Leu Val Ala Leu Pro Arg Thr His Arg Ala Leu Ala
1635 1640 1645
Gly Leu Tyr Pro Arg Thr His Arg Thr His Arg Pro Arg Ala Ser Asn
1650 1655 1660
Gly Leu Tyr Ala Ser Asn Pro Arg Val Ala Leu Ala Ser Pro Gly Leu
1665 1670 1675 1680
Cys Tyr Ser Ala Ser Pro Ala Ser Pro Ala Ser Pro Gly Leu Asn Ala
1685 1690 1695
Leu Ala Ala Ser Asn Cys Tyr Ser His Ile Ser Ser Glu Arg Gly Leu
1700 1705 1710
Tyr Thr His Arg Gly Leu Tyr Ala Ser Pro Ala Ser Pro Pro His Glu
1715 1720 1725
Gly Leu Asn Leu Glu Thr His Arg Gly Leu Tyr Gly Leu Tyr Thr His
1730 1735 1740
Arg Thr His Arg Val Ala Leu Leu Glu Ala Leu Ala Thr His Arg Gly
1745 1750 1755 1760
Leu Leu Tyr Ser Pro Arg Thr His Arg Ile Leu Glu Ile Leu Glu Ala
1765 1770 1775
Ser Pro Ser Glu Arg Thr His Arg Ile Leu Glu Gly Leu Asn Ser Glu
1780 1785 1790
Arg Gly Leu Pro His Glu Pro Arg Thr His Arg Thr Tyr Arg Gly Leu
1795 1800 1805
Tyr Pro His Glu Ala Ser Asn Cys Tyr Ser Gly Leu Pro His Glu Gly
1810 1815 1820
Leu Tyr Thr Arg Pro Gly Leu Tyr Ser Glu Arg His Ile Ser Leu Tyr
1825 1830 1835 1840
Ser Thr His Arg Pro His Glu Cys Tyr Ser His Ile Ser Thr Arg Pro
1845 1850 1855
Gly Leu His Ile Ser Ala Ser Pro Ser Glu Arg His Ile Ser Ala Leu
1860 1865 1870
Ala Gly Leu Asn Leu Glu Ala Arg Gly Thr Arg Pro Ala Arg Gly Val
1875 1880 1885
Ala Leu Leu Glu Thr His Arg Ser Glu Arg Leu Tyr Ser Thr His Arg
1890 1895 1900
Gly Leu Tyr Pro Arg Ile Leu Glu Gly Leu Asn Ala Ser Pro His Ile
1905 1910 1915 1920
Ser Thr His Arg Gly Leu Tyr Ala Ser Pro Gly Leu Tyr Ala Ser Asn
1925 1930 1935
Pro His Glu Ile Leu Glu Thr Tyr Arg Ser Glu Arg Gly Leu Asn Ala
1940 1945 1950
Leu Ala Ala Ser Pro Gly Leu Ala Ser Asn Gly Leu Asn Leu Tyr Ser
1955 1960 1965
Gly Leu Tyr Leu Tyr Ser Val Ala Leu Ala Leu Ala Ala Arg Gly Leu
1970 1975 1980
Glu Val Ala Leu Ser Glu Arg Pro Arg Val Ala Leu Val Ala Leu Thr
1985 1990 1995 2000
Tyr Arg Ser Glu Arg Gly Leu Asn Ser Glu Arg Ser Glu Arg Ala Leu
2005 2010 2015
Ala His Ile Ser Cys Tyr Ser Met Glu Thr Thr His Arg Pro His Glu
2020 2025 2030
Thr Arg Pro Thr Tyr Arg His Ile Ser Met Glu Thr Ser Glu Arg Gly
2035 2040 2045
Leu Tyr Ser Glu Arg His Ile Ser Val Ala Leu Gly Leu Tyr Thr His

```
    2050                2055                2060
Arg Leu Glu Ala Arg Gly Val Ala Leu Leu Tyr Ser Leu Glu His Ile
2065                2070                2075                2080
Ser Thr Tyr Arg Gly Leu Asn Leu Tyr Ser Pro Arg Gly Leu Gly Leu
                2085                2090                2095
Thr Tyr Arg Ala Ser Pro Gly Leu Asn Leu Glu Val Ala Leu Thr Arg
            2100                2105                2110
Pro Met Glu Thr Val Ala Leu Val Ala Leu Gly Leu Tyr His Ile Ser
        2115                2120                2125
Gly Leu Asn Gly Leu Tyr Ala Ser Pro His Ile Ser Thr Arg Pro Leu
    2130                2135                2140
Tyr Ser Gly Leu Gly Leu Tyr Ala Arg Gly Val Ala Leu Leu Glu Leu
2145                2150                2155                2160
Glu His Ile Ser Leu Tyr Ser Ser Glu Arg Leu Glu Leu Tyr Ser Leu
                2165                2170                2175
Glu Thr Tyr Arg Gly Leu Asn Val Ala Leu Ile Leu Glu Pro His Glu
            2180                2185                2190
Gly Leu Gly Leu Tyr Gly Leu Ile Leu Glu Gly Leu Tyr Leu Tyr Ser
        2195                2200                2205
Gly Leu Tyr Ala Ser Asn Leu Glu Gly Leu Tyr Gly Leu Tyr Ile Leu
    2210                2215                2220
Glu Ala Leu Ala Val Ala Leu Ala Ser Pro Ala Ser Pro Ile Leu Glu
2225                2230                2235                2240
Ser Glu Arg Ile Leu Glu Ala Ser Asn Ala Ser Asn His Ile Ser Ile
                2245                2250                2255
Leu Glu Pro Arg Gly Leu Asn Gly Leu Ala Ser Pro Cys Tyr Ser Ala
            2260                2265                2270
Leu Ala Leu Tyr Ser Pro Arg Thr His Arg Ala Ser Pro Leu Glu Ala
        2275                2280                2285
Ser Pro Leu Tyr Ser Leu Tyr Ser Ala Ser Asn Thr His Arg Gly Leu
    2290                2295                2300
Ile Leu Glu Leu Tyr Ser Ile Leu Glu Ala Ser Pro Gly Leu Thr His
2305                2310                2315                2320
Arg Gly Leu Tyr Ser Glu Arg Thr His Arg Pro Arg Gly Leu Tyr Thr
                2325                2330                2335
Tyr Arg Gly Leu Gly Leu Gly Leu Tyr Leu Tyr Ser Gly Leu Tyr Ala
            2340                2345                2350
Ser Pro Leu Tyr Ser Ala Ser Asn Ile Leu Glu Ser Glu Arg Ala Arg
        2355                2360                2365
Gly Leu Tyr Ser Pro Arg Gly Leu Tyr Ala Ser Asn Val Ala Leu Leu
    2370                2375                2380
Glu Leu Tyr Ser Thr His Arg Leu Glu Ala Ser Pro Pro Arg Ile Leu
2385                2390                2395                2400
Glu Leu Glu Ile Leu Glu Thr His Arg Ile Leu Glu Ile Leu Glu Ala
                2405                2410                2415
Leu Ala Met Glu Thr Ser Glu Arg Ala Leu Ala Leu Glu Gly Leu Tyr
            2420                2425                2430
Val Ala Leu Leu Glu Leu Glu Gly Leu Tyr Ala Leu Ala Val Ala Leu
        2435                2440                2445
Cys Tyr Ser Gly Leu Tyr Val Ala Leu Val Ala Leu Leu Glu Thr Tyr
    2450                2455                2460
Arg Cys Tyr Ser Ala Leu Ala Cys Tyr Ser Thr Arg Pro His Ile Ser
2465                2470                2475                2480
Ala Ser Asn Gly Leu Tyr Met Glu Thr Ser Glu Arg Gly Leu Ala Arg
                2485                2490                2495
Gly Ala Ser Asn Leu Glu Ser Glu Arg Ala Leu Ala Leu Glu Gly Leu
            2500                2505                2510
```

Ala Ser Asn Thr Tyr Arg Ala Ser Asn Pro His Glu Gly Leu Leu Glu
2515 2520 2525
Val Ala Leu Ala Ser Pro Gly Leu Tyr Val Ala Leu Leu Tyr Ser Leu
2530 2535 2540
Glu Leu Tyr Ser Leu Tyr Ser Ala Ser Pro Leu Tyr Ser Leu Glu Ala
2545 2550 2555 2560
Ser Asn Pro Arg His Ile Ser Ser Glu Arg Ala Ser Asn Thr Tyr Arg
2565 2570 2575
Ser Glu Arg Gly Leu Ala Leu Ala
2580

mouse SR1

(2) INFORMATION FOR SEQ ID NO:5:
(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 3652 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: double
(D) TOPOLOGY: linear
(ii) MOLECULE TYPE: cDNA
(xi) SEQUENCE DESCRIPTION: SEQ ID NO:5:

TTTTTTTTTT TTTTTTTTTT TTTTTTTTTT TTTTTCCTCC TTCTTCTTCT TCCTGAGACA 60
TGGCCCGGGC AGTGGCTCCT GGAAGAGGAA CAAGTGTGGG AAAAGGGAGA GGAAATCGGA 120
GCTAAATGAC AGGATGCAGG CGACTTGAGA CACAAAAAGA GAAGCGCTTC TCGCGAATTC 180
AGGCATTGCC TCGCCGCTAG CCTTCCCCGC CAAGACCCGC TGAGGATTTT ATGGTTCTTA 240
GGCGGACTTA AGAGCGTTTC GGATTGTTAA GATTATCGTT TGCTGGTTTT TCGTCCGCGC 300
AATCGTGTTC TCCTGCGGCT GCCTGGGGAC TGGCTTGGCG AAGGAGGATG GAGAGGGGGC 360
TGCCGTTGCT GTGCGCCACG CTCGCCCTTG CCCTCGCCCT GGCGGGCGCT TTCCGCAGCG 420
ACAAATGTGG CGGGACCATA AAAATCGAAA ACCCAGGGTA CCTCACATCT CCCGGTTACC 480
CTCATTCTTA CCATCCAAGT GAGAAGTGTG AATGGCTAAT CCAAGCTCCG GAACCCTACC 540
AGAGAATCAT AATCAACTTC AACCCACATT TCGATTTGGA GGACAGAGAC TGCAAGTATG 600
ACTACGTGGA AGTAATTGAT GGGGAGAATG AAGGCGGCCG CCTGTGGGGG AAGTTCTGTG 660
GGAAGATTGC ACCTTCTCCT GTGGTGTCTT CAGGGCCCTT TCTCTTCATC AAATTTGTCT 720
CTGACTATGA GACACATGGG GCAGGGTTTT CCATCCGCTA TGAAATCTTC AAGAGAGGGC 780
CCGAATGTTC TCAGAACTAT ACAGCACCTA CTGGAGTGAT AAAGTCCCCT GGGTTCCCTG 840
AAAAATACCC CAACTGCTTG GAGTGCACCT ACATCATCTT TGCACCAAAG ATGTCTGAGA 900
TAATCCTGGA GTTTGAAAGT TTTGACCTGG AGCAAGACTC GAATCCTCCC GGAGGAATGT 960
TCTGTCGCTA TGACCGGCTG GAGATCTGGG ATGGATTCCC TGAAGTTGGC CCTCACATTG 1020
GGCGTTATTG TGGGCAGAAA ACTCCTGGCC GGATCCGCTC CTCTTCAGGC GTTCTATCCA 1080
TGGTCTTTTA CACTGACAGC GCAATAGCAA AAGAAGGTTT CTCAGCCAAC TACAGTGTGC 1140
TACAGAGCAG CATCTCTGAA GATTTTAAGT GTATGGAGGC TCTGGGCATG GAATCTGGAG 1200
AGATCCATTC TGATCAGATC ACTGCATCTT CACAGTATGG TACCAACTGG TCTGTAGAGC 1260
GCTCCCGCCT GAACTACCCT GAAAATGGGT GGACTCCAGG AGAAGACTCC TACAAGGAGT 1320
GGATCCAGGT GGACTTGGGC CTCCTGCGAT TCGTTACTGC TGTAGGGACA CAGGGTGCCA 1380
TTTCCAAGGA AACCAAGAAG AAATATTATG TCAAGACTTA CAGAGTAGAC ATCAGCTCCA 1440
ACGGAGAGGA CTGGATCTCC CTGAAAGAGG GAAATAAAGC CATTATCTTT CAGGGAAACA 1500
CCAACCCCAC AGATGTTGTC TTAGGAGTTT TCTCCAAACC ACTGATAACT CGATTTGTCC 1560
GAATCAAACC TGTATCCTGG GAAACTGGTA TATCTATGAG ATTTGAAGTT TATGGCTGCA 1620
AGATAACAGA TTATCCTTGC TCTGGAATGT TGGGCATGGT GTCTGGACTT ATTTCAGACT 1680
CCCAGATTAC AGCATCCAAT CAAGCCGACA GGAATTGGAT GCCAGAAAAC ATCCGTCTGG 1740
TGACCAGTCG TACCGGCTGG GCACTGCCAC CCTCACCCCA CCCATACACC AATGAATGGC 1800
TCCAAGTGGA CCTGGGAGAT GAGAAGATAG TAAGAGGTGT CATCATTCAG GGTGGGAAGC 1860
ACCGAGAAAA CAAGGTGTTC ATGAGGAAGT TCAAGATCGC CTATAGTAAC AATGGCTCTG 1920
ACTGGAAAAC TATCATGGAT GACAGCAAGC GCAAGGCTAA GTCGTTCGAA GGCAACAACA 1980
ACTATGACAC ACCTGAGCTT CGGACGTTTT CACCTCTCTC CACAAGGTTC ATCAGGATCT 2040
ACCCTGAGAG AGCCACACAC AGTGGGCTTG GGCTGAGGAT GGAGCTACTG GGCTGTGAAG 2100
TGGAAGCACC TACAGCTGGA CCAACCACAC CCAATGGGAA CCCAGTGCAT GAGTGTGACG 2160
ACGACCAGGC CAACTGCCAC AGTGGCACAG GTGATGACTT CCAGCTCACA GGAGGCACCA 2220
CTGTCCTGGC CACAGAGAAG CCAACCATTA TAGACAGCAC CATCCAATCA GAGTTCCCGA 2280

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CATACGGTTT TAACTGCGAG TTTGGCTGGG GCTCTCACAA GACATTCTGC CACTGGGAGC   2340
ATGACAGCCA TGCACAGCTC AGGTGGAGTG TGCTGACCAG CAAGACAGGG CCGATTCAGG   2400
ACCATACAGG AGATGGCAAC TTCATCTATT CCCAAGCTGA TGAAAATCAG AAAGGCAAAG   2460
TAGCCCGCCT GGTGAGCCCT GTGGTCTATT CCCAGAGCTC TGCCCACTGT ATGACCTTCT   2520
GGTATCACAT GTCCGGCTCT CATGTGGGTA CACTGAGGGT CAAACTACGC TACCAGAAGC   2580
CAGAGGAATA TGATCAACTG GTCTGGATGG TGGTTGGGCA CCAAGGAGAC CACTGGAAAG   2640
AAGGACGTGT CTTGCTGCAC AAATCTCTGA AACTATATCA GGTTATTTTT GAAGGTGAAA   2700
TCGGAAAAGG AAACCTTGGT GGAATTGCTG TGGATGATAT CAGTATTAAC AACCATATTT   2760
CTCAGGAAGA CTGTGCAAAA CCAACAGACC TAGATAAAAA GAACACAGAA ATTAAAATTG   2820
ATGAAACAGG GAGCACTCCA GGATATGAAG GAGAAGGGGA AGGTGACAAG AACATCTCCA   2880
GGAAGCCAGG CAATGTGCTT AAGACCCTGG ATCCCATCCT GATCACCATC ATAGCCATGA   2940
GTGCCCTGGG AGTACTCCTG GGTGCAGTCT GTGGAGTTGT GCTGTACTGT GCCTGTTGGC   3000
ACAATGGGAT GTCAGAAAGG AACCTATCTG CCCTGGAGAA CTATAACTTT GAACTTGTGG   3060
ATGGTGTAAA GTTGAAAAAA GATAAACTGA ACCCACAGAG TAATTACTCA GAGGCGTGAA   3120
GGCACGGAGC TGGAGGGAAC AAGGGAGGAG CACGGCAGGA GAACAGGTGG AGGCATGGGG   3180
ACTCTGTTAC TCTGCTTTCA CTGTAAGCTG GGAAGGGCGG GGACTCTGTT ACTCCGCTTT   3240
CACTGTAAGC TCGGAAGGGC ATCCACGATG CCATGCCAGG CTTTTCTCAG GAGCTTCAAT   3300
GAGCGTCACC TACAGACACA AGCAGGTGAC TGCGGTAACA ACAGGAATCA TGTACAAGCC   3360
TGCTTTCTTC TCTTGGTTTC ATTTGGGTAA TCAGAAGCCA TTTGAGACCA AGTGTGACTG   3420
ACTTCATGGT TCATCCTACT AGCCCCCTTT TTTCCTCTCT TTCTCCTTAC CCTGTGGTGG   3480
ATTCTTCTCG GAAACTGCAA AATCCAAGAT GCTGGCACTA GGCGTTATTC AGTGGGCCCT   3540
TTTGATGGAC ATGTGACCTG TAGCCCAGTG CCCAGAGCAT ATTATCATAA CCACATTTCA   3600
GGGGACGCCA ACGTCCATCC ACCTTTGCAT CGCTACCTGC AGCGAGCACA GG           3652
```

(2) INFORMATION FOR SEQ ID NO:6:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 923 amino acids

(B) TYPE: amino acid

(C) STRANDEDNESS: single

(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:6:

```
Met Glu Arg Gly Leu Pro Leu Leu Cys Ala Thr Leu Ala Leu Ala Leu
1               5                  10                  15
Ala Leu Ala Gly Ala Phe Arg Ser Asp Lys Cys Gly Gly Thr Ile Lys
            20                  25                  30
Ile Glu Asn Pro Gly Tyr Leu Thr Ser Pro Gly Tyr Pro His Ser Tyr
        35                  40                  45
His Pro Ser Glu Lys Cys Glu Trp Leu Ile Gln Ala Pro Glu Pro Tyr
    50                  55                  60
Gln Arg Ile Ile Ile Asn Phe Asn Pro His Phe Asp Leu Glu Asp Arg
65                  70                  75                  80
Asp Cys Lys Tyr Asp Tyr Val Glu Val Ile Asp Gly Glu Asn Glu Gly
                85                  90                  95
Gly Arg Leu Trp Gly Lys Phe Cys Gly Lys Ile Ala Pro Ser Pro Val
            100                 105                 110
Val Ser Ser Gly Pro Phe Leu Phe Ile Lys Phe Val Ser Asp Tyr Glu
        115                 120                 125
Thr His Gly Ala Gly Phe Ser Ile Arg Tyr Glu Ile Phe Lys Arg Gly
    130                 135                 140
Pro Glu Cys Ser Gln Asn Tyr Thr Ala Pro Thr Gly Val Ile Lys Ser
145                 150                 155                 160
Pro Gly Phe Pro Glu Lys Tyr Pro Asn Cys Leu Glu Cys Thr Tyr Ile
                165                 170                 175
Ile Phe Ala Pro Lys Met Ser Glu Ile Ile Leu Glu Phe Glu Ser Phe
            180                 185                 190
Asp Leu Glu Gln Asp Ser Asn Pro Pro Gly Gly Met Phe Cys Arg Tyr
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          195                 200                 205
Asp Arg Leu Glu Ile Trp Asp Gly Phe Pro Glu Val Gly Pro His Ile
      210                 215                 220
Gly Arg Tyr Cys Gly Gln Lys Thr Pro Gly Arg Ile Arg Ser Ser Ser
225                 230                 235                 240
Gly Val Leu Ser Met Val Phe Tyr Thr Asp Ser Ala Ile Ala Lys Glu
                245                 250                 255
Gly Phe Ser Ala Asn Tyr Ser Val Leu Gln Ser Ser Ile Ser Glu Asp
            260                 265                 270
Phe Lys Cys Met Glu Ala Leu Gly Met Glu Ser Gly Glu Ile His Ser
        275                 280                 285
Asp Gln Ile Thr Ala Ser Ser Gln Tyr Gly Thr Asn Trp Ser Val Glu
    290                 295                 300
Arg Ser Arg Leu Asn Tyr Pro Glu Asn Gly Trp Thr Pro Gly Glu Asp
305                 310                 315                 320
Ser Tyr Lys Glu Trp Ile Gln Val Asp Leu Gly Leu Leu Arg Phe Val
                325                 330                 335
Thr Ala Val Gly Thr Gln Gly Ala Ile Ser Lys Glu Thr Lys Lys Lys
            340                 345                 350
Tyr Tyr Val Lys Thr Tyr Arg Val Asp Ile Ser Ser Asn Gly Glu Asp
        355                 360                 365
Trp Ile Ser Leu Lys Glu Gly Asn Lys Ala Ile Ile Phe Gln Gly Asn
    370                 375                 380
Thr Asn Pro Thr Asp Val Val Leu Gly Val Phe Ser Lys Pro Leu Ile
385                 390                 395                 400
Thr Arg Phe Val Arg Ile Lys Pro Val Ser Trp Glu Thr Gly Ile Ser
                405                 410                 415
Met Arg Phe Glu Val Tyr Gly Cys Lys Ile Thr Asp Tyr Pro Cys Ser
            420                 425                 430
Gly Met Leu Gly Met Val Ser Gly Leu Ile Ser Asp Ser Gln Ile Thr
        435                 440                 445
Ala Ser Asn Gln Ala Asp Arg Asn Trp Met Pro Glu Asn Ile Arg Leu
    450                 455                 460
Val Thr Ser Arg Thr Gly Trp Ala Leu Pro Pro Ser Pro His Pro Tyr
465                 470                 475                 480
Thr Asn Glu Trp Leu Gln Val Asp Leu Gly Asp Glu Lys Ile Val Arg
                485                 490                 495
Gly Val Ile Ile Gln Gly Gly Lys His Arg Glu Asn Lys Val Phe Met
            500                 505                 510
Arg Lys Phe Lys Ile Ala Tyr Ser Asn Asn Gly Ser Asp Trp Lys Thr
        515                 520                 525
Ile Met Asp Asp Ser Lys Arg Lys Ala Lys Ser Phe Glu Gly Asn Asn
    530                 535                 540
Asn Tyr Asp Thr Pro Glu Leu Arg Thr Phe Ser Pro Leu Ser Thr Arg
545                 550                 555                 560
Phe Ile Arg Ile Tyr Pro Glu Arg Ala Thr His Ser Gly Leu Gly Leu
                565                 570                 575
Arg Met Glu Leu Leu Gly Cys Glu Val Glu Ala Pro Thr Ala Gly Pro
            580                 585                 590
Thr Thr Pro Asn Gly Asn Pro Val His Glu Cys Asp Asp Asp Gln Ala
        595                 600                 605
Asn Cys His Ser Gly Thr Gly Asp Asp Phe Gln Leu Thr Gly Gly Thr
    610                 615                 620
Thr Val Leu Ala Thr Glu Lys Pro Thr Ile Ile Asp Ser Thr Ile Gln
625                 630                 635                 640
Ser Glu Phe Pro Thr Tyr Gly Phe Asn Cys Glu Phe Gly Trp Gly Ser
                645                 650                 655
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His Lys Thr Phe Cys His Trp Glu His Asp Ser His Ala Gln Leu Arg
                660                 665                 670
Trp Ser Val Leu Thr Ser Lys Thr Gly Pro Ile Gln Asp His Thr Gly
            675                 680                 685
Asp Gly Asn Phe Ile Tyr Ser Gln Ala Asp Glu Asn Gln Lys Gly Lys
    690                 695                 700
Val Ala Arg Leu Val Ser Pro Val Val Tyr Ser Gln Ser Ser Ala His
705                 710                 715                 720
Cys Met Thr Phe Trp Tyr His Met Ser Gly Ser His Val Gly Thr Leu
                725                 730                 735
Arg Val Lys Leu Arg Tyr Gln Lys Pro Glu Glu Tyr Asp Gln Leu Val
                740                 745                 750
Trp Met Val Val Gly His Gln Gly Asp His Trp Lys Glu Gly Arg Val
            755                 760                 765
Leu Leu His Lys Ser Leu Lys Leu Tyr Gln Val Ile Phe Glu Gly Glu
    770                 775                 780
Ile Gly Lys Gly Asn Leu Gly Gly Ile Ala Val Asp Asp Ile Ser Ile
785                 790                 795                 800
Asn Asn His Ile Ser Gln Glu Asp Cys Ala Lys Pro Thr Asp Leu Asp
                805                 810                 815
Lys Lys Asn Thr Glu Ile Lys Ile Asp Glu Thr Gly Ser Thr Pro Gly
                820                 825                 830
Tyr Glu Gly Glu Gly Glu Gly Asp Lys Asn Ile Ser Arg Lys Pro Gly
            835                 840                 845
Asn Val Leu Lys Thr Leu Asp Pro Ile Leu Ile Thr Ile Ile Ala Met
    850                 855                 860
Ser Ala Leu Gly Val Leu Leu Gly Ala Val Cys Gly Val Val Leu Tyr
865                 870                 875                 880
Cys Ala Cys Trp His Asn Gly Met Ser Glu Arg Asn Leu Ser Ala Leu
                885                 890                 895
Glu Asn Tyr Asn Phe Glu Leu Val Asp Gly Val Lys Leu Lys Lys Asp
                900                 905                 910
Lys Leu Asn Pro Gln Ser Asn Tyr Ser Glu Ala
            915                 920
```

(2) INFORMATION FOR SEQ ID NO:7:

rat SR2

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 3539 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: cDNA

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:7:

```
AAACTGGAGC TCCACCGCGG TGGCGGCCGC CCGGGCAGGT CTAGAATTCA GCGGCCGCTG      60
AATTCTATCC AGCGGTCGGT GCCTCTGCCC GCGTGTGTGT CCCGGGTGCC GGGGGACCTG     120
TGTCAGTTAG CGCTTCTGAG ATCACACAGC TGCCTAGGGG CCGTGTGATG CCCAGGGCAA     180
TTCTTGGCTT TGATTTTTAT TATTATTACT ATTATTTTGC GTTCAGCTTT CGGGAAACCC     240
TCGTGATGTT GTAGGATAAA GGAAATGACA CTTTGAGGAA CTGGAGAGAA CATACACGCG     300
TTTGGGTTTG AAGAGGAAAC CGGTCTCCGC TTCCTTAGCT TGCTCCCTCT TTGCTGATTT     360
CAAGAGCTAT CTCCTATGAG GTGGAGATAT TCCAGCAAGA ATAAAGGTGA AGACAGACTG     420
ACTGCCAGGA CCCAGGAGGA AAACGTTGAT CGTTAGAGAC CTTTGCAGAA GACACCACCA     480
GGAGGAAAAT TAGAGAGGAA AAACACAAAG ACATAATTAT ATGGAGATCC CACAAACTTA     540
GCCCGGGAGA GAGCTTCTCT GTCAAAAATG GATATGTTTC CTCTTACCTG GGTTTTCTTA     600
GCTCTGTACT TTTCAGGACA CGAAGTGAGA AGCCAGCAAG ATCCACCTTG CGGAGGTCGG     660
CCGAATTCCA AGGATGCTGG CTACATCACT TCCCCAGGCT ACCCCCAGGA CTATCCCTCC     720
CACCAGAACT GTGAGTGGAT TGTCTACGCC CCCGAACCCA ACCAGAAGAT TGTTCTCAAC     780
TTCAACCCTC ACTTTGAAAT CGAGAAACAC GACTGCAAGT ATGACTTCAT TGAGATTCGG     840
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GATGGGGACA GTGAGTCAGC TGACCTCCTG GGCAAGCACT GTGGGAACAT CGCCCCGCCC     900
ACCATCATCT CCTCAGGCTC CGTGTTATAC ATCAAGTTCA CCTCAGACTA CGCCCGGCAG     960
GGGGCAGGTT TCTCTCTACG CTATGAGATC TTCAAAACAG GCTCTGAAGA TTGTTCCAAG    1020
AACTTTACAA GCCCCAATGG GACCATTGAA TCTCCAGGGT TTCCAGAGAA GTATCCACAC    1080
AATCTGGACT GTACCTTCAC CATCCTGGCC AAACCCAGGA TGGAGATCAT CCTACAGTTC    1140
CTGACCTTTG ACCTGGAGCA TGACCCTCTA CAAGTGGGGG AAGGAGACTG TAAATATGAC    1200
TGGCTGGACA TCTGGGATGG CATTCCACAT GTTGGACCTC TGATTGGCAA GTACTGTGGG    1260
ACGAAAACAC CCTCCAAACT CCGCTCGTCC ACGGGGATCC TCTCCTTGAC CTTTCACACG    1320
GACATGGCAG TGGCCAAGGA TGGCTTCTCC GCACGTTACT ATTTGATCCA CCAGGAGCCA    1380
CCTGAGAATT TTCAGTGCAA TGTCCCTTTG GGAATGGAGT CTGGCCGGAT TGCTAATGAA    1440
CAGATCAGTG CCTCCTCCAC CTTCTCTGAT GGGAGGTGGA CTCCTCAACA GAGCCGGCTC    1500
CATGGTGATG ACAATGGCTG GACACCCAAT TTGGATTCCA ACAAGGAGTA TCTCCAGGTG    1560
GACCTGCGCT TCCTAACCAT GCTCACAGCC ATTGCAACAC AGGGAGCCAT TTCCAGGGAA    1620
ACCCAGAAAG GCTACTACGT CAAATCGTAC AAGCTGGAAG TCAGCACAAA TGGTGAAGAT    1680
TGGATGGTCT ACCGGCATGG CAAAAACCAC AAGATATTCC AAGCGAACAA TGATGCGACC    1740
GAGGTGGTGC TAAACAAGCT CCACATGCCA CTGCTGACTC GGTTCATCAG GATCCGCCCG    1800
CAGACGTGGC ATTTGGGCAT TGCCCTTCGC CTGGAGCTCT TTGGCTGCCG GGTCACAGAT    1860
GCACCCTGCT CCAACATGCT GGGGATGCTC TCGGGCCTCA TTGCTGATAC CCAGATCTCT    1920
GCCTCCTCCA CCCGAGAGTA CCTCTGGAGC CCCAGTGCTG CCCGCCTGGT TAGTAGCCGC    1980
TCTGGCTGGT TTCCTCGGAA CCCTCAAGCC CAGCCAGGTG AAGAATGGCT TCAGGTTGAC    2040
CTGGGGACAC CCAAGACAGT GAAAGGGGTC ATCATCCAGG GAGCCCGAGG AGGAGACAGC    2100
ATCACTGCCG TGGAAGCCAG GGCGTTTGTA CGCAAGTTCA AAGTCTCCTA CAGCCTAAAT    2160
GGCAAGGACT GGGAATATAT CCAGGACCCC AGGACTCAGC AGACAAAGCT GTTTGAAGGG    2220
AACATGCACT ATGACACCCC TGACATCCGA AGGTTCGATC CTGTTCCAGC GCAGTATGTG    2280
CGGGTGTACC CAGAGAGGTG GTCGCCAGCA GGCATCGGGA TGAGGCTGGA GGTGCTGGGC    2340
TGTGACTGGA CAGACTCAAA GCCCACAGTG GAGACGCTGG GACCCACCGT GAAGAGTGAA    2400
GAGACTACCA CCCCATATCC CATGGATGAG GATGCCACCG AGTGTGGGGA AAACTGCAGC    2460
TTTGAGGATG ACAAAGATTT GCAACTTCCT TCAGGATTCA ACTGCAACTT TGATTTTCCG    2520
GAAGAGACCT GTGGTTGGGT GTACGACCAT GCCAAGTGGC TCCGGAGCAC GTGGATCAGC    2580
AGCGCTAACC CCAATGACAG AACATTTCCA GATGACAAGA ACTTCTTGAA ACTGCAGAGT    2640
GATGGCCGAC GAGAGGGCCA GTACGGGCGG CTCATCAGCC CACCGGTGCA CCTGCCCCGA    2700
AGCCCTGTGT GCATGGAGTT CCAGTACCAA GCCATGGGCG GCCACGGGGT GGCACTGCAG    2760
GTGGTTCGGG AAGCCAGCCA GGAAAGCAAA CTCCTTTGGG TCATCCGTGA GGACCAGGGC    2820
AGCGAGTGGA AGCACGGGCG CATTATCCTG CCCAGCTATG ACATGGAGTA TCAGATCGTG    2880
TTCGAGGGAG TGATAGGGAA GGGACGATCG GGAGAGATTT CCATCGATGA CATTCGGATA    2940
AGCACTGATG TCCCACTGGA GAACTGCATG GAACCCATAT CAGCTTTTGC AGATGAATAT    3000
GAAGGAGATT GGAGCAACTC TTCTTCCTCT ACCTCAGGGG CTGGTGACCC CTCATCTGGC    3060
AAAGAAAAGA GCTGGCTGTA CACCCTAGAT CCCATTCTGA TCACCATCAT CGCCATGAGC    3120
TCGCTGGGGG TCCTGCTGGG GGCCACCTGT GCGGGCCTCC TCCTTTACTG CACCTGCTCC    3180
TATTCGGGTC TGAGTTCGAG GAGCTGCACC ACACTGGAGA ACTACAACTT TGAGCTCTAC    3240
GATGGCCTCA AGCACAAGGT CAAGATCAAT CATCAGAAGT GCTGCTCGGA GGCATGACCG    3300
ATTGTGTCTG GATCGCTTCT GGCGTTTCAT TCCAGTGAGA GGGGCTAGCG AAGATTACAG    3360
TTTTGTTTTG TTTTGTTTTG TTTTCCCTTT GGAAACTGAA TGCCATAATC TGGATCAAAG    3420
TGTTCCAGAA TACTGAAGGT ATGGACAGGA CAGACAGGCC AGTCTAGGGA GAAAGGGAGA    3480
TGCAGCTGTG AAGGGGATCG TTGCCCACCA GGACTGTGGT GGCCAAGTGA ATGCAGGAA     3539
```

(2) INFORMATION FOR SEQ ID NO:8:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 909 amino acids

(B) TYPE: amino acid

(C) STRANDEDNESS: single

(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:8:

```
Met Asp Met Phe Pro Leu Thr Trp Val Phe Leu Ala Leu Tyr Phe Ser
1               5                  10                  15
Gly His Glu Val Arg Ser Gln Gln Asp Pro Pro Cys Gly Gly Arg Pro
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                20                  25                  30
Asn Ser Lys Asp Ala Gly Tyr Ile Thr Ser Pro Gly Tyr Pro Gln Asp
        35                  40                  45
Tyr Pro Ser His Gln Asn Cys Glu Trp Ile Val Tyr Ala Pro Glu Pro
    50                  55                  60
Asn Gln Lys Ile Val Leu Asn Phe Asn Pro His Phe Glu Ile Glu Lys
65                  70                  75                  80
His Asp Cys Lys Tyr Asp Phe Ile Glu Ile Arg Asp Gly Asp Ser Glu
                85                  90                  95
Ser Ala Asp Leu Leu Gly Lys His Cys Gly Asn Ile Ala Pro Pro Thr
            100                 105                 110
Ile Ile Ser Ser Gly Ser Val Leu Tyr Ile Lys Phe Thr Ser Asp Tyr
        115                 120                 125
Ala Arg Gln Gly Ala Gly Phe Ser Leu Arg Tyr Glu Ile Phe Lys Thr
    130                 135                 140
Gly Ser Glu Asp Cys Ser Lys Asn Phe Thr Ser Pro Asn Gly Thr Ile
145                 150                 155                 160
Glu Ser Pro Gly Phe Pro Glu Lys Tyr Pro His Asn Leu Asp Cys Thr
                165                 170                 175
Phe Thr Ile Leu Ala Lys Pro Arg Met Glu Ile Ile Leu Gln Phe Leu
            180                 185                 190
Thr Phe Asp Leu Glu His Asp Pro Leu Gln Val Gly Glu Gly Asp Cys
        195                 200                 205
Lys Tyr Asp Trp Leu Asp Ile Trp Asp Gly Ile Pro His Val Gly Pro
    210                 215                 220
Leu Ile Gly Lys Tyr Cys Gly Thr Lys Thr Pro Ser Lys Leu Arg Ser
225                 230                 235                 240
Ser Thr Gly Ile Leu Ser Leu Thr Phe His Thr Asp Met Ala Val Ala
                245                 250                 255
Lys Asp Gly Phe Ser Ala Arg Tyr Tyr Leu Ile His Gln Glu Pro Pro
            260                 265                 270
Glu Asn Phe Gln Cys Asn Val Pro Leu Gly Met Glu Ser Gly Arg Ile
        275                 280                 285
Ala Asn Glu Gln Ile Ser Ala Ser Ser Thr Phe Ser Asp Gly Arg Trp
    290                 295                 300
Thr Pro Gln Gln Ser Arg Leu His Gly Asp Asp Asn Gly Trp Thr Pro
305                 310                 315                 320
Asn Leu Asp Ser Asn Lys Glu Tyr Leu Gln Val Asp Leu Arg Phe Leu
                325                 330                 335
Thr Met Leu Thr Ala Ile Ala Thr Gln Gly Ala Ile Ser Arg Glu Thr
            340                 345                 350
Gln Lys Gly Tyr Tyr Val Lys Ser Tyr Lys Leu Glu Val Ser Thr Asn
        355                 360                 365
Gly Glu Asp Trp Met Val Tyr Arg His Gly Lys Asn His Lys Ile Phe
    370                 375                 380
Gln Ala Asn Asn Asp Ala Thr Glu Val Val Leu Asn Lys Leu His Met
385                 390                 395                 400
Pro Leu Leu Thr Arg Phe Ile Arg Ile Arg Pro Gln Thr Trp His Leu
                405                 410                 415
Gly Ile Ala Leu Arg Leu Glu Leu Phe Gly Cys Arg Val Thr Asp Ala
            420                 425                 430
Pro Cys Ser Asn Met Leu Gly Met Leu Ser Gly Leu Ile Ala Asp Thr
        435                 440                 445
Gln Ile Ser Ala Ser Ser Thr Arg Glu Tyr Leu Trp Ser Pro Ser Ala
    450                 455                 460
Ala Arg Leu Val Ser Ser Arg Ser Gly Trp Phe Pro Arg Asn Pro Gln
465                 470                 475                 480
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Ala Gln Pro Gly Glu Glu Trp Leu Gln Val Asp Leu Gly Thr Pro Lys
                485                 490                 495
Thr Val Lys Gly Val Ile Ile Gln Gly Ala Arg Gly Gly Asp Ser Ile
            500                 505                 510
Thr Ala Val Glu Ala Arg Ala Phe Val Arg Lys Phe Lys Val Ser Tyr
        515                 520                 525
Ser Leu Asn Gly Lys Asp Trp Glu Tyr Ile Gln Asp Pro Arg Thr Gln
    530                 535                 540
Gln Thr Lys Leu Phe Glu Gly Asn Met His Tyr Asp Thr Pro Asp Ile
545                 550                 555                 560
Arg Arg Phe Asp Pro Val Pro Ala Gln Tyr Val Arg Val Tyr Pro Glu
                565                 570                 575
Arg Trp Ser Pro Ala Gly Ile Gly Met Arg Leu Glu Val Leu Gly Cys
            580                 585                 590
Asp Trp Thr Asp Ser Lys Pro Thr Val Glu Thr Leu Gly Pro Thr Val
        595                 600                 605
Lys Ser Glu Glu Thr Thr Thr Pro Tyr Pro Met Asp Glu Asp Ala Thr
    610                 615                 620
Glu Cys Gly Glu Asn Cys Ser Phe Glu Asp Asp Lys Asp Leu Gln Leu
625                 630                 635                 640
Pro Ser Gly Phe Asn Cys Asn Phe Asp Phe Pro Glu Glu Thr Cys Gly
                645                 650                 655
Trp Val Tyr Asp His Ala Lys Trp Leu Arg Ser Thr Trp Ile Ser Ser
            660                 665                 670
Ala Asn Pro Asn Asp Arg Thr Phe Pro Asp Asp Lys Asn Phe Leu Lys
        675                 680                 685
Leu Gln Ser Asp Gly Arg Arg Glu Gly Gln Tyr Gly Arg Leu Ile Ser
    690                 695                 700
Pro Pro Val His Leu Pro Arg Ser Pro Val Cys Met Glu Phe Gln Tyr
705                 710                 715                 720
Gln Ala Met Gly Gly His Gly Val Ala Leu Gln Val Val Arg Glu Ala
                725                 730                 735
Ser Gln Glu Ser Lys Leu Leu Trp Val Ile Arg Glu Asp Gln Gly Ser
            740                 745                 750
Glu Trp Lys His Gly Arg Ile Ile Leu Pro Ser Tyr Asp Met Glu Tyr
        755                 760                 765
Gln Ile Val Phe Glu Gly Val Ile Gly Lys Gly Arg Ser Gly Glu Ile
    770                 775                 780
Ser Ile Asp Asp Ile Arg Ile Ser Thr Asp Val Pro Leu Glu Asn Cys
785                 790                 795                 800
Met Glu Pro Ile Ser Ala Phe Ala Asp Glu Tyr Glu Gly Asp Trp Ser
                805                 810                 815
Asn Ser Ser Ser Ser Thr Ser Gly Ala Gly Asp Pro Ser Ser Gly Lys
            820                 825                 830
Glu Lys Ser Trp Leu Tyr Thr Leu Asp Pro Ile Leu Ile Thr Ile Ile
        835                 840                 845
Ala Met Ser Ser Leu Gly Val Leu Leu Gly Ala Thr Cys Ala Gly Leu
    850                 855                 860
Leu Leu Tyr Cys Thr Cys Ser Tyr Ser Gly Leu Ser Ser Arg Ser Cys
865                 870                 875                 880
Thr Thr Leu Glu Asn Tyr Asn Phe Glu Leu Tyr Asp Gly Leu Lys His
                885                 890                 895
Lys Val Lys Ile Asn His Gln Lys Cys Cys Ser Glu Ala
            900                 905
```

(2) INFORMATION FOR SEQ ID NO:9:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 4718 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: double
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: cDNA

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:9:

```
AAACTGGAGC TCCACCGCGG TGGCGGCCGC CCGGGCAGGT CTAGAATTCA GCGGCCGCTG      60
AATTCTATCC AGCGGTCGGT GCCTCTGCCC GCGTGTGTGT CCCGGGTGCC GGGGGACCTG     120
TGTCAGTTAG CGCTTCTGAG ATCACACAGC TGCCTAGGGG CCGTGTGATG CCCAGGGCAA     180
TTCTTGGCTT TGATTTTTAT TATTATTACT ATTATTTTGC GTTCAGCTTT CGGGAAACCC     240
TCGTGATGTT GTAGGATAAA GGAAATGACA CTTTGAGGAA CTGGAGAGAA CATACACGCG     300
TTTGGGTTTG AAGAGGAAAC CGGTCTCCGC TTCCTTAGCT TGCTCCCTCT TTGCTGATTT     360
CAAGAGCTAT CTCCTATGAG GTGGAGATAT TCCAGCAAGA ATAAAGGTGA AGACAGACTG     420
ACTGCCAGGA CCCAGGAGGA AAACGTTGAT CGTTAGAGAC CTTTGCAGAA GACACCACCA     480
GGAGGAAAAT TAGAGAGGAA AAACACAAAG ACATAATTAT AGGAGATCCC ACAAACCTAG     540
CCCGGGAGAG AGCCTCTCTG TCAAAAATGG ATATGTTTCC TCTTACCTGG GTTTTCTTAG     600
CTCTGTACTT TTCAGGACAC GAAGTGAGAA GCCAGCAAGA TCCACCCTGC GGAGGTCGGC     660
CGAATTCCAA AGATGCTGGC TACATCACTT CCCCAGGCTA CCCCCAGGAC TATCCCTCCC     720
ACCAGAACTG TGAGTGGATT GTCTACGCCC CCGAACCCAA CCAGAAGATT GTTCTCAACT     780
TCAACCCTCA CTTTGAAATC GAGAAACACG ACTGCAAGTA TGACTTCATT GAGATTCGGG     840
ATGGGGACAG TGAGTCAGCT GACCTCCTGG GCAAGCACTG TGGGAACATC GCCCCGCCCA     900
CCATCATCTC CTCAGGCTCC GTGTTATACA TCAAGTTCAC CTCAGACTAC GCCCGGCAGG     960
GGGCAGGTTT CTCTCTACGC TATGAGATCT TCAAAACAGG CTCTGAAGAT TGTTCCAAGA    1020
ACTTTACAAG CCCCAATGGG ACCATTGAAT CTCCAGGGTT TCCAGAGAAG TATCCACACA    1080
ATCTGGACTG TACCTTCACC ATCCTGGCCA AACCCAGGAT GGAGATCATC CTACAGTTCC    1140
TGACCTTTGA CCTGGAGCAT GACCCTCTAC AAGTGGGGGA AGGAGACTGT AAATATGACT    1200
GGCTGGACAT CTGGGATGGC ATTCCACATG TTGGACCTCT GATTGGCAAG TACTGTGGGA    1260
CGAAAACACC CTCCAAACTC CGCTCGTCCA CGGGGATCCT CTCCTTGACC TTTCACACGG    1320
ACATGGCAGT GGCCAAGGAT GGCTTCTCCG CACGTTACTA TTTGATCCAC CAGGAGCCAC    1380
CTGAGAATTT TCAGTGCAAT GTCCCTTTGG GAATGGAGTC TGGCCGGATT GCTAATGAAC    1440
AGATCAGTGC CTCCTCCACC TTCTCTGATG GGAGGTGGAC TCCTCAACAG AGCCGGCTCC    1500
ATGGTGATGA CAATGGCTGG ACACCCAATT TGGATTCCAA CAAGGAGTAT CTCCAGGTGG    1560
ACCTGCGCTT CCTAACCATG CTCACAGCCA TTGCAACACA GGGAGCCATT TCCAGGGAAA    1620
CCCAGAAAGG CTACTACGTC AAATCGTACA AGCTGGAAGT CAGCACAAAT GGTGAAGATT    1680
GGATGGTCTA CCGGCATGGC AAAAACCACA AGATATTCCA AGCGAACAAT GATGCGACCG    1740
AGGTGGTGCT AAACAAGCTC CACATGCCAC TGCTGACTCG GTTCATCAGG ATCCGCCCGC    1800
AGACGTGGCA TTTGGGCATT GCCCTTCGCC TGGAGCTCTT TGGCTGCCGG GTCACAGATG    1860
CACCCTGCTC CAACATGCTG GGGATGCTCT CGGGCCTCAT TGCTGATACC CAGATCTCTG    1920
CCTCCTCCAC CCGAGAGTAC CTCTGGAGCC CCAGTGCTGC CCGCCTGGTT AGTAGCCGCT    1980
CTGGCTGGTT TCCTCGGAAC CCTCAAGCCC AGCCAGGTGA AGAATGGCTT CAGGTAGACC    2040
TGGGGACACC CAAGACAGTG AAAGGGGTCA TCATCCAGGG AGCCCGAGGA GGAGACAGCA    2100
TCACTGCCGT GGAAGCCAGG GCGTTTGTAC GCAAGTTCAA AGTCTCCTAC AGCCTAAATG    2160
GCAAGGACTG GGAATATATC CAGGACCCCA GGACTCAGCA GACAAAGCTG TTTGAAGGGA    2220
ACATGCACTA TGACACCCCT GACATCCGAA GGTTCGATCC TGTTCCAGCG CAGTATGTGC    2280
GGGTGTACCC AGAGAGGTGG TCGCCAGCAG GCATCGGGAT GAGGCTGGAG GTGCTGGGCT    2340
GTGACTGGAC AGACTCAAAG CCCACAGTGG AGACGCTGGG ACCCACCGTG AAGAGTGAAG    2400
AGACTACCAC CCCATATCCC ATGGATGAGG ATGCCACCGA GTGTGGGGAA AACTGCAGCT    2460
TTGAGGATGA CAAAGATTTG CAACTTCCTT CAGGATTCAA CTGCAACTTT GATTTTCCGG    2520
AAGAGACCTG TGGTTGGGTG TACGACCATG CCAAGTGGCT CCGGAGCACG TGGATCAGCA    2580
GCGCTAACCC CAATGACAGA ACATTTCCAG ATGACAAGAA CTTCTTGAAA CTGCAGAGTG    2640
ATGGCCGACG AGAGGGCCAG TACGGGCGGC TCATCAGCCC ACCGGTGCAC CTGCCCCGAA    2700
GCCCTGTGTG CATGGAGTTC CAGTACCAAG CCATGGGCGG CCACGGGGTG GCACTGCAGG    2760
TGGTTCGGGA AGCCAGCCAG GAAAGCAAAC TCCTTTGGGT CATCCGTGAG GACCAGGGCA    2820
GCGAGTGGAA GCACGGGCGC ATTATCCTGC CCAGCTATGA CATGGAGTAT CAGATCGTGT    2880
TCGAGGGAGT GATAGGGAAG GGACGATCGG GAGAGATTTC CGGCGATGAC ATTCGGATAA    2940
GCACTGATGT CCCACTGGAG AACTGCATGG AACCCATATC AGCTTTTGCA GATGAATATG    3000
AAGGAGATTG GAGCAACTCT TCTTCCTCTA CCTCAGGGGC TGGTGACCCC TCATCTGGCA    3060
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AAGAAAAGAG CTGGCTGTAC ACCCTAGATC CCATTCTGAT CACCATCATC GCCATGAGCT    3120
CGCTGGGGGT CCTGCTGGGG GCCACCTGTG CGGGCCTCCT CCTTTACTGC ACCTGCTCCT    3180
ATTCGGGTCT GAGTTCGAGG AGCTGCACCA CACTGGAGAA CTACAACTTT GAGCTCTACG    3240
ATGGCCTCAA GCACAAGGTC AAGATCAATC ATCAGAAGTG CTGCTCGGAG GCATGACCGA    3300
TTGTGTCTGG ATCGCTTCTG GCGTTTCATT CCAGTGAGAG GGGCTAGCGA AGATTACAGT    3360
TTTGTTTTGT TTTGTTTTGT TTTCCCTTTG GAAACTGAAT GCCATAATCT GGATCAAAGT    3420
GTTCCAGAAT ACTGAAGGTA TGGACAGGAC AGACAGGCCA GTCTAGGGAG AAAGGGAGAT    3480
GCAGCTGTGA AGGGGATCGT TGCCCACCAG GACTGTGGTG GCCAAGTGAA TGCAGGAACC    3540
GGGCCCGGAA TTCCGGCTCT CGGCTAAAAT CTCAGCTGCC TCTGGAAAGG CTCAACCATA    3600
CTCAGTGCCA ACTCAGACTC TGTTGCTGTG GTGTCAACAT GGATGGATCA TCTGTACCTT    3660
GTATTTTTAG CAGAATTCAT GCTCAGATTT CTTTGTTCTG AATCCTTGCT TTGTGCTAGA    3720
CACAAAGCAT ACATGTCCTT CTAAAATTAA TATGATCACT ATAATCTCCT GTGTGCAGAA    3780
TTCAGAAATA GACCTTTGAA ACCATTTGCA TTGTGAGTGC AGATCCATGA CTGGGGCTAG    3840
TGCAGCAATG AAACAGAATT CCAGAAACAG TGTGTTCTTT TTATTATGGG AAAATACAGA    3900
TAAAAATGGC CACTGATGAA CATGAAAGTT AGCACTTTCC CAACACAGTG TACACTTGCA    3960
ACCTTGTTTT GGATTTCTCA TACACCAAGA CTGTGAAACA CAAATTTCAA GAATGTGTTC    4020
AAATGTGTGT GTGTGTGTGT GTGTGTGTGT GTGTGTGTGT GTATGTGTGT GTGTGTGTGT    4080
GTGCTTGTGT GTTTCTGTCA GTGGTATGAG TGATATGTAT GCATGTGTGT ATGTATATGT    4140
ATGTATGTAT GTATGTATGT ACGTACATAT GTATGTATGT ATGTATGTAT GTATGTATGT    4200
ATATGTGTGT GTGTGTTTGT GTGTGTGTGT GTTTGTGTGT GTGTGTGTGG TAAGTGTGGT    4260
ATGTGTGTAT GCATTTGTCT ATATGTGTAT CTGTGTGTCT ATGTGTTTCT GTCAGTGGAA    4320
TGAGTGGCAT GTGTGCATGT GTATGTATGT GGATATGTGT GTTGTGTTTA TGTGCTTGTG    4380
TATAAGAGGT AAGTGTGGTG TGTGTGCATG TGTCTCTGTG TGTGTTTGTC TGTGTACCTC    4440
TTTGTATAAG TACCTGTGTT TGTATGTGGG AATATGTATA TTGAGGCATT GCTGTGTTAG    4500
TATGTTTATA GAAAAGAAGA CAGTCTGAGA TGTCTTCCTC AATACCTCTC CACTTATATC    4560
TTGGATAGAC AAAAGTAATG ACAAAAAATT GCTGGTGTGT ATATGGAAAA GGGGGACACA    4620
TATCCATGGA TGGTAGAAGT GTAAACTGTG CAGTCACTGT GGACATCAAT ATGCAGGTTC    4680
TTCACAAATG TAGATATAAA GCTACTATAG TTATACCC                            4718
```

(2) INFORMATION FOR SEQ ID NO:10:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 909 amino acids

(B) TYPE: amino acid

(C) STRANDEDNESS: single

(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:10:

```
Met Asp Met Phe Pro Leu Thr Trp Val Phe Leu Ala Leu Tyr Phe Ser
1               5                  10                  15
Gly His Glu Val Arg Ser Gln Gln Asp Pro Pro Cys Gly Gly Arg Pro
            20                  25                  30
Asn Ser Lys Asp Ala Gly Tyr Ile Thr Ser Pro Gly Tyr Pro Gln Asp
        35                  40                  45
Tyr Pro Ser His Gln Asn Cys Glu Trp Ile Val Tyr Ala Pro Glu Pro
    50                  55                  60
Asn Gln Lys Ile Val Leu Asn Phe Asn Pro His Phe Glu Ile Glu Lys
65                  70                  75                  80
His Asp Cys Lys Tyr Asp Phe Ile Glu Ile Arg Asp Gly Asp Ser Glu
                85                  90                  95
Ser Ala Asp Leu Leu Gly Lys His Cys Gly Asn Ile Ala Pro Pro Thr
            100                 105                 110
Ile Ile Ser Ser Gly Ser Val Leu Tyr Ile Lys Phe Thr Ser Asp Tyr
        115                 120                 125
Ala Arg Gln Gly Ala Gly Phe Ser Leu Arg Tyr Glu Ile Phe Lys Thr
    130                 135                 140
Gly Ser Glu Asp Cys Ser Lys Asn Phe Thr Ser Pro Asn Gly Thr Ile
145                 150                 155                 160
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Glu Ser Pro Gly Phe Pro Glu Lys Tyr Pro His Asn Leu Asp Cys Thr
                165                 170                 175
Phe Thr Ile Leu Ala Lys Pro Arg Met Glu Ile Ile Leu Gln Phe Leu
            180                 185                 190
Thr Phe Asp Leu Glu His Asp Pro Leu Gln Val Gly Glu Gly Asp Cys
        195                 200                 205
Lys Tyr Asp Trp Leu Asp Ile Trp Asp Gly Ile Pro His Val Gly Pro
    210                 215                 220
Leu Ile Gly Lys Tyr Cys Gly Thr Lys Thr Pro Ser Lys Leu Arg Ser
225                 230                 235                 240
Ser Thr Gly Ile Leu Ser Leu Thr Phe His Thr Asp Met Ala Val Ala
                245                 250                 255
Lys Asp Gly Phe Ser Ala Arg Tyr Tyr Leu Ile His Gln Glu Pro Pro
            260                 265                 270
Glu Asn Phe Gln Cys Asn Val Pro Leu Gly Met Glu Ser Gly Arg Ile
        275                 280                 285
Ala Asn Glu Gln Ile Ser Ala Ser Ser Thr Phe Ser Asp Gly Arg Trp
    290                 295                 300
Thr Pro Gln Gln Ser Arg Leu His Gly Asp Asp Asn Gly Trp Thr Pro
305                 310                 315                 320
Asn Leu Asp Ser Asn Lys Glu Tyr Leu Gln Val Asp Leu Arg Phe Leu
                325                 330                 335
Thr Met Leu Thr Ala Ile Ala Thr Gln Gly Ala Ile Ser Arg Glu Thr
            340                 345                 350
Gln Lys Gly Tyr Tyr Val Lys Ser Tyr Lys Leu Glu Val Ser Thr Asn
        355                 360                 365
Gly Glu Asp Trp Met Val Tyr Arg His Gly Lys Asn His Lys Ile Phe
    370                 375                 380
Gln Ala Asn Asn Asp Ala Thr Glu Val Val Leu Asn Lys Leu His Met
385                 390                 395                 400
Pro Leu Leu Thr Arg Phe Ile Arg Ile Arg Pro Gln Thr Trp His Leu
                405                 410                 415
Gly Ile Ala Leu Arg Leu Glu Leu Phe Gly Cys Arg Val Thr Asp Ala
            420                 425                 430
Pro Cys Ser Asn Met Leu Gly Met Leu Ser Gly Leu Ile Ala Asp Thr
        435                 440                 445
Gln Ile Ser Ala Ser Ser Thr Arg Glu Tyr Leu Trp Ser Pro Ser Ala
    450                 455                 460
Ala Arg Leu Val Ser Ser Arg Ser Gly Trp Phe Pro Arg Asn Pro Gln
465                 470                 475                 480
Ala Gln Pro Gly Glu Glu Trp Leu Gln Val Asp Leu Gly Thr Pro Lys
                485                 490                 495
Thr Val Lys Gly Val Ile Ile Gln Gly Ala Arg Gly Gly Asp Ser Ile
            500                 505                 510
Thr Ala Val Glu Ala Arg Ala Phe Val Arg Lys Phe Lys Val Ser Tyr
        515                 520                 525
Ser Leu Asn Gly Lys Asp Trp Glu Tyr Ile Gln Asp Pro Arg Thr Gln
    530                 535                 540
Gln Thr Lys Leu Phe Glu Gly Asn Met His Tyr Asp Thr Pro Asp Ile
545                 550                 555                 560
Arg Arg Phe Asp Pro Val Pro Ala Gln Tyr Val Arg Val Tyr Pro Glu
                565                 570                 575
Arg Trp Ser Pro Ala Gly Ile Gly Met Arg Leu Glu Val Leu Gly Cys
            580                 585                 590
Asp Trp Thr Asp Ser Lys Pro Thr Val Glu Thr Leu Gly Pro Thr Val
        595                 600                 605
Lys Ser Glu Glu Thr Thr Thr Pro Tyr Pro Met Asp Glu Asp Ala Thr
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     610                 615                 620
Glu Cys Gly Glu Asn Cys Ser Phe Glu Asp Asp Lys Asp Leu Gln Leu
625                 630                 635                 640
Pro Ser Gly Phe Asn Cys Asn Phe Asp Phe Pro Glu Glu Thr Cys Gly
                645                 650                 655
Trp Val Tyr Asp His Ala Lys Trp Leu Arg Ser Thr Trp Ile Ser Ser
            660                 665                 670
Ala Asn Pro Asn Asp Arg Thr Phe Pro Asp Asp Lys Asn Phe Leu Lys
        675                 680                 685
Leu Gln Ser Asp Gly Arg Arg Glu Gly Gln Tyr Gly Arg Leu Ile Ser
    690                 695                 700
Pro Pro Val His Leu Pro Arg Ser Pro Val Cys Met Glu Phe Gln Tyr
705                 710                 715                 720
Gln Ala Met Gly Gly His Gly Val Ala Leu Gln Val Val Arg Glu Ala
                725                 730                 735
Ser Gln Glu Ser Lys Leu Leu Trp Val Ile Arg Glu Asp Gln Gly Ser
            740                 745                 750
Glu Trp Lys His Gly Arg Ile Ile Leu Pro Ser Tyr Asp Met Glu Tyr
        755                 760                 765
Gln Ile Val Phe Glu Gly Val Ile Gly Lys Gly Arg Ser Gly Glu Ile
    770                 775                 780
Ser Gly Asp Asp Ile Arg Ile Ser Thr Asp Val Pro Leu Glu Asn Cys
785                 790                 795                 800
Met Glu Pro Ile Ser Ala Phe Ala Asp Glu Tyr Glu Gly Asp Trp Ser
                805                 810                 815
Asn Ser Ser Ser Ser Thr Ser Gly Ala Gly Asp Pro Ser Ser Gly Lys
            820                 825                 830
Glu Lys Ser Trp Leu Tyr Thr Leu Asp Pro Ile Leu Ile Thr Ile Ile
        835                 840                 845
Ala Met Ser Ser Leu Gly Val Leu Leu Gly Ala Thr Cys Ala Gly Leu
    850                 855                 860
Leu Leu Tyr Cys Thr Cys Ser Tyr Ser Gly Leu Ser Ser Arg Ser Cys
865                 870                 875                 880
Thr Thr Leu Glu Asn Tyr Asn Phe Glu Leu Tyr Asp Gly Leu Lys His
                885                 890                 895
Lys Val Lys Ile Asn His Gln Lys Cys Cys Ser Glu Ala
            900                 905
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(2) INFORMATION FOR SEQ ID NO:11:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 4733 base pairs

(B) TYPE: nucleic acid

(C) STRANDEDNESS: double

(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: cDNA

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:11:

```
AAACTGGAGC TCCACCGCGG TGGCGGCCGC CCGGGCAGGT CTAGAATTCA GCGGCCGCTG      60
AATTCTATCC AGCGGTCGGT GCCTCTGCCC GCGTGTGTGT CCCGGGTGCC GGGGGACCTG     120
TGTCAGTTAG CGCTTCTGAG ATCACACAGC TGCCTAGGGG CCGTGTGATG CCCAGGGCAA     180
TTCTTGGCTT TGATTTTTAT TATTATTACT ATTATTTTGC GTTCAGCTTT CGGGAAACCC     240
TCGTGATGTT GTAGGATAAA GGAAATGACA CTTTGAGGAA CTGGAGAGAA CATACACGCG     300
TTTGGGTTTG AAGAGGAAAC CGGTCTCCGC TTCCTTAGCT TGCTCCCTCT TTGCTGATTT     360
CAAGAGCTAT CTCCTATGAG GTGGAGATAT TCCAGCAAGA ATAAAGGTGA AGACAGACTG     420
ACTGCCAGGA CCCAGGAGGA AAACGTTGAT CGTTAGAGAC CTTTGCAGAA GACACCACCA     480
GGAGGAAAAT TAGAGAGGAA AAACACAAAG ACATAATTAT AGGAGATCCC ACAAACCTAG     540
CCCGGGAGAG AGCCTCTCTG TCAAAAATGG ATATGTTTCC TCTTACCTGG GTTTTCTTAG     600
CTCTGTACTT TTCAGGACAC GAAGTGAGAA GCCAGCAAGA TCCACCCTGC GGAGGTCGGC     660
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Move SR2(a)5

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CGAATTCCAA AGATGCTGGC TACATCACTT CCCCAGGCTA CCCCCAGGAC TATCCCTCCC   720
ACCAGAACTG TGAGTGGATT GTCTACGCCC CCGAACCCAA CCAGAAGATT GTTCTCAACT   780
TCAACCCTCA CTTTGAAATC GAGAAACACG ACTGCAAGTA TGACTTCATT GAGATTCGGG   840
ATGGGGACAG TGAGTCAGCT GACCTCCTGG GCAAGCACTG TGGGAACATC GCCCCGCCCA   900
CCATCATCTC CTCAGGCTCC GTGTTATACA TCAAGTTCAC CTCAGACTAC GCCCGGCAGG   960
GGGCAGGTTT CTCTCTACGC TATGAGATCT TCAAAACAGG CTCTGAAGAT TGTTCCAAGA  1020
ACTTTACAAG CCCCAATGGG ACCATTGAAT CTCCAGGGTT TCCAGAGAAG TATCCACACA  1080
ATCTGGACTG TACCTTCACC ATCCTGGCCA AACCCAGGAT GGAGATCATC CTACAGTTCC  1140
TGACCTTTGA CCTGGAGCAT GACCCTCTAC AAGTGGGGGA AGGAGACTGT AAATATGACT  1200
GGCTGGACAT CTGGGATGGC ATTCCACATG TTGGACCTCT GATTGGCAAG TACTGTGGGA  1260
CGAAAACACC CTCCAAACTC CGCTCGTCCA CGGGGATCCT CTCCTTGACC TTTCACACGG  1320
ACATGGCAGT GGCCAAGGAT GGCTTCTCCG CACGTTACTA TTTGATCCAC CAGGAGCCAC  1380
CTGAGAATTT TCAGTGCAAT GTCCCTTTGG GAATGGAGTC TGGCCGGATT GCTAATGAAC  1440
AGATCAGTGC CTCCTCCACC TTCTCTGATG GGAGGTGGAC TCCTCAACAG AGCCGGCTCC  1500
ATGGTGATGA CAATGGCTGG ACACCCAATT TGGATTCCAA CAAGGAGTAT CTCCAGGTGG  1560
ACCTGCGCTT CCTAACCATG CTCACAGCCA TTGCAACACA GGGAGCCATT TCCAGGGAAA  1620
CCCAGAAAGG CTACTACGTC AAATCGTACA AGCTGGAAGT CAGCACAAAT GGTGAAGATT  1680
GGATGGTCTA CCGGCATGGC AAAAACCACA AGATATTCCA AGCGAACAAT GATGCGACCG  1740
AGGTGGTGCT AAACAAGCTC CACATGCCAC TGCTGACTCG GTTCATCAGG ATCCGCCCGC  1800
AGACGTGGCA TTTGGGCATT GCCCTTCGCC TGGAGCTCTT TGGCTGCCGG GTCACAGATG  1860
CACCCTGCTC CAACATGCTG GGGATGCTCT CGGGCCTCAT TGCTGATACC CAGATCTCTG  1920
CCTCCTCCAC CCGAGAGTAC CTCTGGAGCC CCAGTGCTGC CCGCCTGGTT AGTAGCCGCT  1980
CTGGCTGGTT TCCTCGGAAC CCTCAAGCCC AGCCAGGTGA AGAATGGCTT CAGGTAGACC  2040
TGGGGACACC CAAGACAGTG AAAGGGGTCA TCATCCAGGG AGCCCGAGGA GGAGACAGCA  2100
TCACTGCCGT GGAAGCCAGG GCGTTTGTAC GCAAGTTCAA AGTCTCCTAC AGCCTAAATG  2160
GCAAGGACTG GGAATATATC CAGGACCCCA GGACTCAGCA GACAAAGCTG TTTGAAGGGA  2220
ACATGCACTA TGACACCCCT GACATCCGAA GGTTCGATCC TGTTCCAGCG CAGTATGTGC  2280
GGGTGTACCC AGAGAGGTGG TCGCCAGCAG GCATCGGGAT GAGGCTGGAG GTGCTGGGCT  2340
GTGACTGGAC AGACTCAAAG CCCACAGTGG AGACGCTGGG ACCCACCGTG AAGAGTGAAG  2400
AGACTACCAC CCCATATCCC ATGGATGAGG ATGCCACCGA GTGTGGGGAA AACTGCAGCT  2460
TTGAGGATGA CAAAGATTTG CAACTTCCTT CAGGATTCAA CTGCAACTTT GATTTTCCGG  2520
AAGAGACCTG TGGTTGGGTG TACGACCATG CCAAGTGGCT CCGGAGCACG TGGATCAGCA  2580
GCGCTAACCC CAATGACAGA ACATTTCCAG ATGACAAGAA CTTCTTGAAA CTGCAGAGTG  2640
ATGGCCGACG AGAGGGCCAG TACGGGCGGC TCATCAGCCC ACCGGTGCAC CTGCCCCGAA  2700
GCCCTGTGTG CATGGAGTTC CAGTACCAAG CCATGGGCGG CCACGGGGTG GCACTGCAGG  2760
TGGTTCGGGA AGCCAGCCAG GAAAGCAAAC TCCTTTGGGT CATCCGTGAG GACCAGGGCA  2820
GCGAGTGGAA GCACGGGCGC ATTATCCTGC CCAGCTATGA CATGGAGTAT CAGATCGTGT  2880
TCGAGGGAGT GATAGGGAAG GGACGATCGG GAGAGATTTC CGGCGATGAC ATTCGGATAA  2940
GCACTGATGT CCCACTGGAG AACTGCATGG AACCCATATC AGCTTTTGCA GGTGAGGATT  3000
TTAAAGATGA ATATGAAGGA GATTGGAGCA ACTCTTCTTC CTCTACCTCA GGGGCTGGTG  3060
ACCCCTCATC TGGCAAAGAA AAGAGCTGGC TGTACACCCT AGATCCCATT CTGATCACCA  3120
TCATCGCCAT GAGCTCGCTG GGGGTCCTGC TGGGGGCCAC CTGTGCGGGC CTCCTCCTTT  3180
ACTGCACCTG CTCCTATTCG GGTCTGAGTT CGAGGAGCTG CACCACACTG GAGAACTACA  3240
ACTTTGAGCT CTACGATGGC CTCAAGCACA AGGTCAAGAT CAATCATCAG AAGTGCTGCT  3300
CGGAGGCATG ACCGATTGTG TCTGGATCGC TTCTGGCGTT TCATTCCAGT GAGAGGGGCT  3360
AGCGAAGATT ACAGTTTTGT TTTGTTTTGT TTTGTTTTCC CTTTGGAAAC TGAATGCCAT  3420
AATCTGGATC AAAGTGTTCC AGAATACTGA AGGTATGGAC AGGACAGACA GGCCAGTCTA  3480
GGGAGAAAGG GAGATGCAGC TGTGAAGGGG ATCGTTGCCC ACCAGGACTG TGGTGGCCAA  3540
GTGAATGCAG GAACCGGGCC CGGAATTCCG GCTCTCGGCT AAAATCTCAG CTGCCTCTGG  3600
AAAGGCTCAA CCATACTCAG TGCCAACTCA GACTCTGTTG CTGTGGTGTC AACATGGATG  3660
GATCATCTGT ACCTTGTATT TTTAGCAGAA TTCATGCTCA GATTTCTTTG TTCTGAATCC  3720
TTGCTTTGTG CTAGACACAA AGCATACATG TCCTTCTAAA ATTAATATGA TCACTATAAT  3780
CTCCTGTGTG CAGAATTCAG AAATAGACCT TTGAAACCAT TTGCATTGTG AGTGCAGATC  3840
CATGACTGGG GCTAGTGCAG CAATGAAACA GAATTCCAGA AACAGTGTGT TCTTTTTATT  3900
ATGGGAAAAT ACAGATAAAA ATGGCCACTG ATGAACATGA AAGTTAGCAC TTTCCCAACA  3960
CAGTGTACAC TTGCAACCTT GTTTTGGATT TCTCATACAC CAAGACTGTG AAACACAAAT  4020
TTCAAGAATG TGTTCAAATG TGTGTGTGTG TGTGTGTGTG TGTGTGTGTG TGTGTGTATG  4080
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TGTGTGTGTG TGTGTGTGCT TGTGTGTTTC TGTCAGTGGT ATGAGTGATA TGTATGCATG 4140
TGTGTATGTA TATGTATGTA TGTATGTATG TATGTACGTA CATATGTATG TATGTATGTA 4200
TGTATGTATG TATGTATATG TGTGTGTGTG TTTGTGTGTG TGTGTGTTTG TGTGTGTGTG 4260
TGTGGTAAGT GTGGTATGTG TGTATGCATT TGTCTATATG TGTATCTGTG TGTCTATGTG 4320
TTTCTGTCAG TGGAATGAGT GGCATGTGTG CATGTGTATG TATGTGGATA TGTGTGTTGT 4380
GTTTATGTGC TTGTGTATAA GAGGTAAGTG TGGTGTGTGT GCATGTGTCT CTGTGTGTGT 4440
TTGTCTGTGT ACCTCTTTGT ATAAGTACCT GTGTTTGTAT GTGGGAATAT GTATATTGAG 4500
GCATTGCTGT GTTAGTATGT TTATAGAAAA GAAGACAGTC TGAGATGTCT TCCTCAATAC 4560
CTCTCCACTT ATATCTTGGA TAGACAAAAG TAATGACAAA AAATTGCTGG TGTGTATATG 4620
GAAAAGGGGG ACACATATCC ATGGATGGTA GAAGTGTAAA CTGTGCAGTC ACTGTGGACA 4680
TCAATATGCA GGTTCTTCAC AAATGTAGAT ATAAAGCTAC TATAGTTATA CCC 4733

(2) INFORMATION FOR SEQ ID NO:12:
(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 914 amino acids
(B) TYPE: amino acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear
(ii) MOLECULE TYPE: peptide
(xi) SEQUENCE DESCRIPTION: SEQ ID NO:12:

Met Asp Met Phe Pro Leu Thr Trp Val Phe Leu Ala Leu Tyr Phe Ser
1 5 10 15
Gly His Glu Val Arg Ser Gln Gln Asp Pro Pro Cys Gly Gly Arg Pro
20 25 30
Asn Ser Lys Asp Ala Gly Tyr Ile Thr Ser Pro Gly Tyr Pro Gln Asp
35 40 45
Tyr Pro Ser His Gln Asn Cys Glu Trp Ile Val Tyr Ala Pro Glu Pro
50 55 60
Asn Gln Lys Ile Val Leu Asn Phe Asn Pro His Phe Glu Ile Glu Lys
65 70 75 80
His Asp Cys Lys Tyr Asp Phe Ile Glu Ile Arg Asp Gly Asp Ser Glu
85 90 95
Ser Ala Asp Leu Leu Gly Lys His Cys Gly Asn Ile Ala Pro Pro Thr
100 105 110
Ile Ile Ser Ser Gly Ser Val Leu Tyr Ile Lys Phe Thr Ser Asp Tyr
115 120 125
Ala Arg Gln Gly Ala Gly Phe Ser Leu Arg Tyr Glu Ile Phe Lys Thr
130 135 140
Gly Ser Glu Asp Cys Ser Lys Asn Phe Thr Ser Pro Asn Gly Thr Ile
145 150 155 160
Glu Ser Pro Gly Phe Pro Glu Lys Tyr Pro His Asn Leu Asp Cys Thr
165 170 175
Phe Thr Ile Leu Ala Lys Pro Arg Met Glu Ile Ile Leu Gln Phe Leu
180 185 190
Thr Phe Asp Leu Glu His Asp Pro Leu Gln Val Gly Glu Gly Asp Cys
195 200 205
Lys Tyr Asp Trp Leu Asp Ile Trp Asp Gly Ile Pro His Val Gly Pro
210 215 220
Leu Ile Gly Lys Tyr Cys Gly Thr Lys Thr Pro Ser Lys Leu Arg Ser
225 230 235 240
Ser Thr Gly Ile Leu Ser Leu Thr Phe His Thr Asp Met Ala Val Ala
245 250 255
Lys Asp Gly Phe Ser Ala Arg Tyr Tyr Leu Ile His Gln Glu Pro Pro
260 265 270
Glu Asn Phe Gln Cys Asn Val Pro Leu Gly Met Glu Ser Gly Arg Ile
275 280 285
Ala Asn Glu Gln Ile Ser Ala Ser Ser Thr Phe Ser Asp Gly Arg Trp

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    290                 295                 300
Thr Pro Gln Gln Ser Arg Leu His Gly Asp Asp Asn Gly Trp Thr Pro
305                 310                 315                 320
Asn Leu Asp Ser Asn Lys Glu Tyr Leu Gln Val Asp Leu Arg Phe Leu
                325                 330                 335
Thr Met Leu Thr Ala Ile Ala Thr Gln Gly Ala Ile Ser Arg Glu Thr
            340                 345                 350
Gln Lys Gly Tyr Tyr Val Lys Ser Tyr Lys Leu Glu Val Ser Thr Asn
        355                 360                 365
Gly Glu Asp Trp Met Val Tyr Arg His Gly Lys Asn His Lys Ile Phe
    370                 375                 380
Gln Ala Asn Asn Asp Ala Thr Glu Val Val Leu Asn Lys Leu His Met
385                 390                 395                 400
Pro Leu Leu Thr Arg Phe Ile Arg Ile Arg Pro Gln Thr Trp His Leu
                405                 410                 415
Gly Ile Ala Leu Arg Leu Glu Leu Phe Gly Cys Arg Val Thr Asp Ala
            420                 425                 430
Pro Cys Ser Asn Met Leu Gly Met Leu Ser Gly Leu Ile Ala Asp Thr
        435                 440                 445
Gln Ile Ser Ala Ser Ser Thr Arg Glu Tyr Leu Trp Ser Pro Ser Ala
    450                 455                 460
Ala Arg Leu Val Ser Ser Arg Ser Gly Trp Phe Pro Arg Asn Pro Gln
465                 470                 475                 480
Ala Gln Pro Gly Glu Glu Trp Leu Gln Val Asp Leu Gly Thr Pro Lys
                485                 490                 495
Thr Val Lys Gly Val Ile Ile Gln Gly Ala Arg Gly Gly Asp Ser Ile
            500                 505                 510
Thr Ala Val Glu Ala Arg Ala Phe Val Arg Lys Phe Lys Val Ser Tyr
        515                 520                 525
Ser Leu Asn Gly Lys Asp Trp Glu Tyr Ile Gln Asp Pro Arg Thr Gln
    530                 535                 540
Gln Thr Lys Leu Phe Glu Gly Asn Met His Tyr Asp Thr Pro Asp Ile
545                 550                 555                 560
Arg Arg Phe Asp Pro Val Pro Ala Gln Tyr Val Arg Val Tyr Pro Glu
                565                 570                 575
Arg Trp Ser Pro Ala Gly Ile Gly Met Arg Leu Glu Val Leu Gly Cys
            580                 585                 590
Asp Trp Thr Asp Ser Lys Pro Thr Val Glu Thr Leu Gly Pro Thr Val
        595                 600                 605
Lys Ser Glu Glu Thr Thr Thr Pro Tyr Pro Met Asp Glu Asp Ala Thr
    610                 615                 620
Glu Cys Gly Glu Asn Cys Ser Phe Glu Asp Asp Lys Asp Leu Gln Leu
625                 630                 635                 640
Pro Ser Gly Phe Asn Cys Asn Phe Asp Phe Pro Glu Glu Thr Cys Gly
                645                 650                 655
Trp Val Tyr Asp His Ala Lys Trp Leu Arg Ser Thr Trp Ile Ser Ser
            660                 665                 670
Ala Asn Pro Asn Asp Arg Thr Phe Pro Asp Asp Lys Asn Phe Leu Lys
        675                 680                 685
Leu Gln Ser Asp Gly Arg Arg Glu Gly Gln Tyr Gly Arg Leu Ile Ser
    690                 695                 700
Pro Pro Val His Leu Pro Arg Ser Pro Val Cys Met Glu Phe Gln Tyr
705                 710                 715                 720
Gln Ala Met Gly Gly His Gly Val Ala Leu Gln Val Val Arg Glu Ala
                725                 730                 735
Ser Gln Glu Ser Lys Leu Leu Trp Val Ile Arg Glu Asp Gln Gly Ser
            740                 745                 750
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Glu Trp Lys His Gly Arg Ile Ile Leu Pro Ser Tyr Asp Met Glu Tyr
        755                 760                 765
Gln Ile Val Phe Glu Gly Val Ile Gly Lys Gly Arg Ser Gly Glu Ile
    770                 775                 780
Ser Gly Asp Asp Ile Arg Ile Ser Thr Asp Val Pro Leu Glu Asn Cys
785                 790                 795                 800
Met Glu Pro Ile Ser Ala Phe Ala Gly Glu Asp Phe Lys Asp Glu Tyr
                805                 810                 815
Glu Gly Asp Trp Ser Asn Ser Ser Ser Ser Thr Ser Gly Ala Gly Asp
            820                 825                 830
Pro Ser Ser Gly Lys Glu Lys Ser Trp Leu Tyr Thr Leu Asp Pro Ile
        835                 840                 845
Leu Ile Thr Ile Ile Ala Met Ser Ser Leu Gly Val Leu Leu Gly Ala
    850                 855                 860
Thr Cys Ala Gly Leu Leu Leu Tyr Cys Thr Cys Ser Tyr Ser Gly Leu
865                 870                 875                 880
Ser Ser Arg Ser Cys Thr Thr Leu Glu Asn Tyr Asn Phe Glu Leu Tyr
                885                 890                 895
Asp Gly Leu Lys His Lys Val Lys Ile Asn His Gln Lys Cys Cys Ser
            900                 905                 910
Glu Ala
```

more SR2(a) ?

(2) INFORMATION FOR SEQ ID NO:13:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 4769 base pairs

(B) TYPE: nucleic acid

(C) STRANDEDNESS: single

(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: cDNA

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:13:

```
AAACTGGAGC TCCACCGCGG TGGCGGCCGC CCGGGCAGGT CTAGAATTCA GCGGCCGCTG      60
AATTCTATCC AGCGGTCGGT GCCTCTGCCC GCGTGTGTGT CCCGGGTGCC GGGGGACCTG     120
TGTCAGTTAG CGCTTCTGAG ATCACACAGC TGCCTAGGGG CCGTGTGATG CCCAGGGCAA     180
TTCTTGGCTT TGATTTTTAT TATTATTACT ATTATTTTGC GTTCAGCTTT CGGGAAACCC     240
TCGTGATGTT GTAGGATAAA GGAAATGACA CTTTGAGGAA CTGGAGAGAA CATACACGCG     300
TTTGGGTTTG AAGAGGAAAC CGGTCTCCGC TTCCTTAGCT TGCTCCCTCT TTGCTGATTT     360
CAAGAGCTAT CTCCTATGAG GTGGAGATAT TCCAGCAAGA ATAAAGGTGA AGACAGACTG     420
ACTGCCAGGA CCCAGGAGGA AAACGTTGAT CGTTAGAGAC CTTTGCAGAA GACACCACCA     480
GGAGGAAAAT TAGAGAGGAA AAACACAAAG ACATAATTAT AGGAGATCCC ACAAACCTAG     540
CCCGGGAGAG AGCCTCTCTG TCAAAAATGG ATATGTTTCC TCTTACCTGG GTTTTCTTAG     600
CTCTGTACTT TTCAGGACAC GAAGTGAGAA GCCAGCAAGA TCCACCCTGC GGAGGTCGGC     660
CGAATTCCAA AGATGCTGGC TACATCACTT CCCCAGGCTA CCCCCAGGAC TATCCCTCCC     720
ACCAGAACTG TGAGTGGATT GTCTACGCCC CCGAACCCAA CCAGAAGATT GTTCTCAACT     780
TCAACCCTCA CTTTGAAATC GAGAAACACG ACTGCAAGTA TGACTTCATT GAGATTCGGG     840
ATGGGGACAG TGAGTCAGCT GACCTCCTGG GCAAGCACTG TGGGAACATC GCCCCGCCCA     900
CCATCATCTC CTCAGGCTCC GTGTTATACA TCAAGTTCAC CTCAGACTAC GCCCGGCAGG     960
GGGCAGGTTT CTCTCTACGC TATGAGATCT TCAAAACAGG CTCTGAAGAT TGTTCCAAGA    1020
ACTTTACAAG CCCCAATGGG ACCATTGAAT CTCCAGGGTT TCCAGAGAAG TATCCACACA    1080
ATCTGGACTG TACCTTCACC ATCCTGGCCA AACCCAGGAT GGAGATCATC CTACAGTTCC    1140
TGACCTTTGA CCTGGAGCAT GACCCTCTAC AAGTGGGGGA AGGAGACTGT AAATATGACT    1200
GGCTGGACAT CTGGGATGGC ATTCCACATG TTGGACCTCT GATTGGCAAG TACTGTGGGA    1260
CGAAAACACC CTCCAAACTC CGCTCGTCCA CGGGGATCCT CTCCTTGACC TTTCACACGG    1320
ACATGGCAGT GGCCAAGGAT GGCTTCTCCG CACGTTACTA TTTGATCCAC CAGGAGCCAC    1380
CTGAGAATTT TCAGTGCAAT GTCCCTTTGG GAATGGAGTC TGGCCGGATT GCTAATGAAC    1440
AGATCAGTGC CTCCTCCACC TTCTCTGATG GGAGGTGGAC TCCTCAACAG AGCCGGCTCC    1500
ATGGTGATGA CAATGGCTGG ACACCCAATT TGGATTCCAA CAAGGAGTAT CTCCAGGTGG    1560
ACCTGCGCTT CCTAACCATG CTCACAGCCA TTGCAACACA GGGAGCCATT TCCAGGGAAA    1620
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CCCAGAAAGG CTACTACGTC AAATCGTACA AGCTGGAAGT CAGCACAAAT GGTGAAGATT    1680
GGATGGTCTA CCGGCATGGC AAAAACCACA AGATATTCCA AGCGAACAAT GATGCGACCG    1740
AGGTGGTGCT AAACAAGCTC CACATGCCAC TGCTGACTCG GTTCATCAGG ATCCGCCCGC    1800
AGACGTGGCA TTTGGGCATT GCCCTTCGCC TGGAGCTCTT TGGCTGCCGG GTCACAGATG    1860
CACCCTGCTC CAACATGCTG GGGATGCTCT CGGGCCTCAT TGCTGATACC CAGATCTCTG    1920
CCTCCTCCAC CCGAGAGTAC CTCTGGAGCC CCAGTGCTGC CCGCCTGGTT AGTAGCCGCT    1980
CTGGCTGGTT TCCTCGGAAC CCTCAAGCCC AGCCAGGTGA AGAATGGCTT CAGGTAGACC    2040
TGGGGACACC CAAGACAGTG AAAGGGGTCA TCATCCAGGG AGCCCGAGGA GGAGACAGCA    2100
TCACTGCCGT GGAAGCCAGG GCGTTTGTAC GCAAGTTCAA AGTCTCCTAC AGCCTAAATG    2160
GCAAGGACTG GGAATATATC CAGGACCCCA GGACTCAGCA GACAAAGCTG TTTGAAGGGA    2220
ACATGCACTA TGACACCCCT GACATCCGAA GGTTCGATCC TGTTCCAGCG CAGTATGTGC    2280
GGGTGTACCC AGAGAGGTGG TCGCCAGCAG GCATCGGGAT GAGGCTGGAG GTGCTGGGCT    2340
GTGACTGGAC AGACTCAAAG CCCACAGTGG AGACGCTGGG ACCCACCGTG AAGAGTGAAG    2400
AGACTACCAC CCCATATCCC ATGGATGAGG ATGCCACCGA GTGTGGGGAA AACTGCAGCT    2460
TTGAGGATGA CAAAGATTTG CAACTTCCTT CAGGATTCAA CTGCAACTTT GATTTTCCGG    2520
AAGAGACCTG TGGTTGGGTG TACGACCATG CCAAGTGGCT CCGGAGCACG TGGATCAGCA    2580
GCGCTAACCC CAATGACAGA ACATTTCCAG ATGACAAGAA CTTCTTGAAA CTGCAGAGTG    2640
ATGGCCGACG AGAGGGCCAG TACGGGCGGC TCATCAGCCC ACCGGTGCAC CTGCCCCGAA    2700
GCCCTGTGTG CATGGAGTTC CAGTACCAAG CCATGGGCGG CCACGGGGTG GCACTGCAGG    2760
TGGTTCGGGA AGCCAGCCAG GAAAGCAAAC TCCTTTGGGT CATCCGTGAG GACCAGGGCA    2820
GCGAGTGGAA GCACGGGCGC ATTATCCTGC CCAGCTATGA CATGGAGTAT CAGATCGTGT    2880
TCGAGGGAGT GATAGGGAAG GGACGATCGG GAGAGATTTC CGGCGATGAC ATTCGGATAA    2940
GCACTGATGT CCCACTGGAG AACTGCATGG AACCCATATC AGCTTTTGCA GTGGACATCC    3000
CAGAAACCCA TGGGGGAGAG GGCTATGAAG ATGAGATTGA TGATGAATAT GAAGGAGATT    3060
GGAGCAACTC TTCTTCCTCT ACCTCAGGGG CTGGTGACCC CTCATCTGGC AAAGAAAAGA    3120
GCTGGCTGTA CACCCTAGAT CCCATTCTGA TCACCATCAT CGCCATGAGC TCGCTGGGGG    3180
TCCTGCTGGG GGCCACCTGT GCGGGCCTCC TCCTTTACTG CACCTGCTCC TATTCGGGTC    3240
TGAGTTCGAG GAGCTGCACC ACACTGGAGA ACTACAACTT TGAGCTCTAC GATGGCCTCA    3300
AGCACAAGGT CAAGATCAAT CATCAGAAGT GCTGCTCGGA GGCATGACCG ATTGTGTCTG    3360
GATCGCTTCT GGCGTTTCAT TCCAGTGAGA GGGGCTAGCG AAGATTACAG TTTTGTTTTG    3420
TTTTGTTTTG TTTTCCCTTT GGAAACTGAA TGCCATAATC TGGATCAAAG TGTTCCAGAA    3480
TACTGAAGGT ATGGACAGGA CAGACAGGCC AGTCTAGGGA GAAAGGGAGA TGCAGCTGTG    3540
AAGGGGATCG TTGCCCACCA GGACTGTGGT GGCCAAGTGA ATGCAGGAAC CGGGCCCGGA    3600
ATTCCGGCTC TCGGCTAAAA TCTCAGCTGC CTCTGGAAAG GCTCAACCAT ACTCAGTGCC    3660
AACTCAGACT CTGTTGCTGT GGTGTCAACA TGGATGGATC ATCTGTACCT TGTATTTTTA    3720
GCAGAATTCA TGCTCAGATT TCTTTGTTCT GAATCCTTGC TTTGTGCTAG ACACAAAGCA    3780
TACATGTCCT TCTAAAATTA ATATGATCAC TATAATCTCC TGTGTGCAGA ATTCAGAAAT    3840
AGACCTTTGA AACCATTTGC ATTGTGAGTG CAGATCCATG ACTGGGGCTA GTGCAGCAAT    3900
GAAACAGAAT TCCAGAAACA GTGTGTTCTT TTTATTATGG GAAAATACAG ATAAAAATGG    3960
CCACTGATGA ACATGAAAGT TAGCACTTTC CCAACACAGT GTACACTTGC AACCTTGTTT    4020
TGGATTTCTC ATACACCAAG ACTGTGAAAC ACAAATTTCA AGAATGTGTT CAAATGTGTG    4080
TGTGTGTGTG TGTGTGTGTG TGTGTGTGTG TGTATGTGTG TGTGTGTGTG TGTGCTTGTG    4140
TGTTTCTGTC AGTGGTATGA GTGATATGTA TGCATGTGTG TATGTATATG TATGTATGTA    4200
TGTATGTATG TACGTACATA TGTATGTATG TATGTATGTA TGTATGTATG TATATGTGTG    4260
TGTGTGTTTG TGTGTGTGTG TGTTTGTGTG TGTGTGTGTG GTAAGTGTGG TATGTGTGTA    4320
TGCATTTGTC TATATGTGTA TCTGTGTGTC TATGTGTTTC TGTCAGTGGA ATGAGTGGCA    4380
TGTGTGCATG TGTATGTATG TGGATATGTG TGTTGTGTTT ATGTGCTTGT GTATAAGAGG    4440
TAAGTGTGGT GTGTGTGCAT GTGTCTCTGT GTGTGTTTGT CTGTGTACCT CTTTGTATAA    4500
GTACCTGTGT TTGTATGTGG GAATATGTAT ATTGAGGCAT TGCTGTGTTA GTATGTTTAT    4560
AGAAAAGAAG ACAGTCTGAG ATGTCTTCCT CAATACCTCT CCACTTATAT CTTGGATAGA    4620
CAAAAGTAAT GACAAAAAAT TGCTGGTGTG TATATGGAAA AGGGGGACAC ATATCCATGG    4680
ATGGTAGAAG TGTAAACTGT GCAGTCACTG TGGACATCAA TATGCAGGTT CTTCACAAAT    4740
GTAGATATAA AGCTACTATA GTTATACCC                                      4769
```

(2) INFORMATION FOR SEQ ID NO:14:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 926 amino acids

(B) TYPE: amino acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:14:

```
Met Asp Met Phe Pro Leu Thr Trp Val Phe Leu Ala Leu Tyr Phe Ser
1               5                  10                  15
Gly His Glu Val Arg Ser Gln Gln Asp Pro Pro Cys Gly Gly Arg Pro
            20                  25                  30
Asn Ser Lys Asp Ala Gly Tyr Ile Thr Ser Pro Gly Tyr Pro Gln Asp
        35                  40                  45
Tyr Pro Ser His Gln Asn Cys Glu Trp Ile Val Tyr Ala Pro Glu Pro
    50                  55                  60
Asn Gln Lys Ile Val Leu Asn Phe Asn Pro His Phe Glu Ile Glu Lys
65                  70                  75                  80
His Asp Cys Lys Tyr Asp Phe Ile Glu Ile Arg Asp Gly Asp Ser Glu
                85                  90                  95
Ser Ala Asp Leu Leu Gly Lys His Cys Gly Asn Ile Ala Pro Pro Thr
            100                 105                 110
Ile Ile Ser Ser Gly Ser Val Leu Tyr Ile Lys Phe Thr Ser Asp Tyr
        115                 120                 125
Ala Arg Gln Gly Ala Gly Phe Ser Leu Arg Tyr Glu Ile Phe Lys Thr
    130                 135                 140
Gly Ser Glu Asp Cys Ser Lys Asn Phe Thr Ser Pro Asn Gly Thr Ile
145                 150                 155                 160
Glu Ser Pro Gly Phe Pro Glu Lys Tyr Pro His Asn Leu Asp Cys Thr
                165                 170                 175
Phe Thr Ile Leu Ala Lys Pro Arg Met Glu Ile Ile Leu Gln Phe Leu
            180                 185                 190
Thr Phe Asp Leu Glu His Asp Pro Leu Gln Val Gly Glu Gly Asp Cys
        195                 200                 205
Lys Tyr Asp Trp Leu Asp Ile Trp Asp Gly Ile Pro His Val Gly Pro
    210                 215                 220
Leu Ile Gly Lys Tyr Cys Gly Thr Lys Thr Pro Ser Lys Leu Arg Ser
225                 230                 235                 240
Ser Thr Gly Ile Leu Ser Leu Thr Phe His Thr Asp Met Ala Val Ala
                245                 250                 255
Lys Asp Gly Phe Ser Ala Arg Tyr Tyr Leu Ile His Gln Glu Pro Pro
            260                 265                 270
Glu Asn Phe Gln Cys Asn Val Pro Leu Gly Met Glu Ser Gly Arg Ile
        275                 280                 285
Ala Asn Glu Gln Ile Ser Ala Ser Ser Thr Phe Ser Asp Gly Arg Trp
    290                 295                 300
Thr Pro Gln Gln Ser Arg Leu His Gly Asp Asp Asn Gly Trp Thr Pro
305                 310                 315                 320
Asn Leu Asp Ser Asn Lys Glu Tyr Leu Gln Val Asp Leu Arg Phe Leu
                325                 330                 335
Thr Met Leu Thr Ala Ile Ala Thr Gln Gly Ala Ile Ser Arg Glu Thr
            340                 345                 350
Gln Lys Gly Tyr Tyr Val Lys Ser Tyr Lys Leu Glu Val Ser Thr Asn
        355                 360                 365
Gly Glu Asp Trp Met Val Tyr Arg His Gly Lys Asn His Lys Ile Phe
    370                 375                 380
Gln Ala Asn Asn Asp Ala Thr Glu Val Val Leu Asn Lys Leu His Met
385                 390                 395                 400
Pro Leu Leu Thr Arg Phe Ile Arg Ile Arg Pro Gln Thr Trp His Leu
                405                 410                 415
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Gly Ile Ala Leu Arg Leu Glu Leu Phe Gly Cys Arg Val Thr Asp Ala
            420                 425                 430
Pro Cys Ser Asn Met Leu Gly Met Leu Ser Gly Leu Ile Ala Asp Thr
        435                 440                 445
Gln Ile Ser Ala Ser Ser Thr Arg Glu Tyr Leu Trp Ser Pro Ser Ala
    450                 455                 460
Ala Arg Leu Val Ser Ser Arg Ser Gly Trp Phe Pro Arg Asn Pro Gln
465                 470                 475                 480
Ala Gln Pro Gly Glu Glu Trp Leu Gln Val Asp Leu Gly Thr Pro Lys
                485                 490                 495
Thr Val Lys Gly Val Ile Ile Gln Gly Ala Arg Gly Gly Asp Ser Ile
            500                 505                 510
Thr Ala Val Glu Ala Arg Ala Phe Val Arg Lys Phe Lys Val Ser Tyr
        515                 520                 525
Ser Leu Asn Gly Lys Asp Trp Glu Tyr Ile Gln Asp Pro Arg Thr Gln
    530                 535                 540
Gln Thr Lys Leu Phe Glu Gly Asn Met His Tyr Asp Thr Pro Asp Ile
545                 550                 555                 560
Arg Arg Phe Asp Pro Val Pro Ala Gln Tyr Val Arg Val Tyr Pro Glu
                565                 570                 575
Arg Trp Ser Pro Ala Gly Ile Gly Met Arg Leu Glu Val Leu Gly Cys
            580                 585                 590
Asp Trp Thr Asp Ser Lys Pro Thr Val Glu Thr Leu Gly Pro Thr Val
        595                 600                 605
Lys Ser Glu Glu Thr Thr Thr Pro Tyr Pro Met Asp Glu Asp Ala Thr
    610                 615                 620
Glu Cys Gly Glu Asn Cys Ser Phe Glu Asp Asp Lys Asp Leu Gln Leu
625                 630                 635                 640
Pro Ser Gly Phe Asn Cys Asn Phe Asp Phe Pro Glu Glu Thr Cys Gly
                645                 650                 655
Trp Val Tyr Asp His Ala Lys Trp Leu Arg Ser Thr Trp Ile Ser Ser
            660                 665                 670
Ala Asn Pro Asn Asp Arg Thr Phe Pro Asp Asp Lys Asn Phe Leu Lys
        675                 680                 685
Leu Gln Ser Asp Gly Arg Arg Glu Gly Gln Tyr Gly Arg Leu Ile Ser
    690                 695                 700
Pro Pro Val His Leu Pro Arg Ser Pro Val Cys Met Glu Phe Gln Tyr
705                 710                 715                 720
Gln Ala Met Gly Gly His Gly Val Ala Leu Gln Val Val Arg Glu Ala
                725                 730                 735
Ser Gln Glu Ser Lys Leu Leu Trp Val Ile Arg Glu Asp Gln Gly Ser
            740                 745                 750
Glu Trp Lys His Gly Arg Ile Ile Leu Pro Ser Tyr Asp Met Glu Tyr
        755                 760                 765
Gln Ile Val Phe Glu Gly Val Ile Gly Lys Gly Arg Ser Gly Glu Ile
    770                 775                 780
Ser Gly Asp Asp Ile Arg Ile Ser Thr Asp Val Pro Leu Glu Asn Cys
785                 790                 795                 800
Met Glu Pro Ile Ser Ala Phe Ala Val Asp Ile Pro Glu Thr His Gly
                805                 810                 815
Gly Glu Gly Tyr Glu Asp Glu Ile Asp Asp Glu Tyr Glu Gly Asp Trp
            820                 825                 830
Ser Asn Ser Ser Ser Ser Thr Ser Gly Ala Gly Asp Pro Ser Ser Gly
        835                 840                 845
Lys Glu Lys Ser Trp Leu Tyr Thr Leu Asp Pro Ile Leu Ile Thr Ile
    850                 855                 860
Ile Ala Met Ser Ser Leu Gly Val Leu Leu Gly Ala Thr Cys Ala Gly
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865                 870                 875                 880
Leu Leu Leu Tyr Cys Thr Cys Ser Tyr Ser Gly Leu Ser Ser Arg Ser
                885                 890                 895
Cys Thr Thr Leu Glu Asn Tyr Asn Phe Glu Leu Tyr Asp Gly Leu Lys
            900                 905                 910
His Lys Val Lys Ile Asn His Gln Lys Cys Cys Ser Glu Ala
        915                 920                 925
```

(2) INFORMATION FOR SEQ ID NO:15:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 4784 base pairs

(B) TYPE: nucleic acid

(C) STRANDEDNESS: single

(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: cDNA

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:15:

mouse SEQ(6)22

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AAACTGGAGC TCCACCGCGG TGGCGGCCGC CCGGGCAGGT CTAGAATTCA GCGGCCGCTG      60
AATTCTATCC AGCGGTCGGT GCCTCTGCCC GCGTGTGTGT CCCGGGTGCC GGGGGACCTG     120
TGTCAGTTAG CGCTTCTGAG ATCACACAGC TGCCTAGGGG CCGTGTGATG CCCAGGGCAA     180
TTCTTGGCTT TGATTTTTAT TATTATTACT ATTATTTTGC GTTCAGCTTT CGGGAAACCC     240
TCGTGATGTT GTAGGATAAA GGAAATGACA CTTTGAGGAA CTGGAGAGAA CATACACGCG     300
TTTGGGTTTG AAGAGGAAAC CGGTCTCCGC TTCCTTAGCT TGCTCCCTCT TTGCTGATTT     360
CAAGAGCTAT CTCCTATGAG GTGGAGATAT TCCAGCAAGA ATAAAGGTGA AGACAGACTG     420
ACTGCCAGGA CCCAGGAGGA AAACGTTGAT CGTTAGAGAC CTTTGCAGAA GACACCACCA     480
GGAGGAAAAT TAGAGAGGAA AAACACAAAG ACATAATTAT AGGAGATCCC ACAAACCTAG     540
CCCGGGAGAG AGCCTCTCTG TCAAAAATGG ATATGTTTCC TCTTACCTGG GTTTTCTTAG     600
CTCTGTACTT TTCAGGACAC GAAGTGAGAA GCCAGCAAGA TCCACCCTGC GGAGGTCGGC     660
CGAATTCCAA AGATGCTGGC TACATCACTT CCCCAGGCTA CCCCCAGGAC TATCCCTCCC     720
ACCAGAACTG TGAGTGGATT GTCTACGCCC CCGAACCCAA CCAGAAGATT GTTCTCAACT     780
TCAACCCTCA CTTTGAAATC GAGAAACACG ACTGCAAGTA TGACTTCATT GAGATTCGGG     840
ATGGGGACAG TGAGTCAGCT GACCTCCTGG GCAAGCACTG TGGGAACATC GCCCCGCCCA     900
CCATCATCTC CTCAGGCTCC GTGTTATACA TCAAGTTCAC CTCAGACTAC GCCCGGCAGG     960
GGGCAGGTTT CTCTCTACGC TATGAGATCT TCAAAACAGG CTCTGAAGAT TGTTCCAAGA    1020
ACTTTACAAG CCCCAATGGG ACCATTGAAT CTCCAGGGTT TCCAGAGAAG TATCCACACA    1080
ATCTGGACTG TACCTTCACC ATCCTGGCCA AACCCAGGAT GGAGATCATC CTACAGTTCC    1140
TGACCTTTGA CCTGGAGCAT GACCCTCTAC AAGTGGGGGA AGGAGACTGT AAATATGACT    1200
GGCTGGACAT CTGGGATGGC ATTCCACATG TTGGACCTCT GATTGGCAAG TACTGTGGGA    1260
CGAAAACACC CTCCAAACTC CGCTCGTCCA CGGGGATCCT CTCCTTGACC TTTCACACGG    1320
ACATGGCAGT GGCCAAGGAT GGCTTCTCCG CACGTTACTA TTTGATCCAC CAGGAGCCAC    1380
CTGAGAATTT TCAGTGCAAT GTCCCTTTGG GAATGGAGTC TGGCCGGATT GCTAATGAAC    1440
AGATCAGTGC CTCCTCCACC TTCTCTGATG GGAGGTGGAC TCCTCAACAG AGCCGGCTCC    1500
ATGGTGATGA CAATGGCTGG ACACCCAATT TGGATTCCAA CAAGGAGTAT CTCCAGGTGG    1560
ACCTGCGCTT CCTAACCATG CTCACAGCCA TTGCAACACA GGGAGCCATT TCCAGGGAAA    1620
CCCAGAAAGG CTACTACGTC AAATCGTACA AGCTGGAAGT CAGCACAAAT GGTGAAGATT    1680
GGATGGTCTA CCGGCATGGC AAAAACCACA AGATATTCCA AGCGAACAAT GATGCGACCG    1740
AGGTGGTGCT AAACAAGCTC CACATGCCAC TGCTGACTCG GTTCATCAGG ATCCGCCCGC    1800
AGACGTGGCA TTTGGGCATT GCCCTTCGCC TGGAGCTCTT TGGCTGCCGG GTCACAGATG    1860
CACCCTGCTC CAACATGCTG GGGATGCTCT CGGGCCTCAT TGCTGATACC CAGATCTCTG    1920
CCTCCTCCAC CCGAGAGTAC CTCTGGAGCC CCAGTGCTGC CCGCCTGGTT AGTAGCCGCT    1980
CTGGCTGGTT TCCTCGGAAC CCTCAAGCCC AGCCAGGTGA AGAATGGCTT CAGGTAGACC    2040
TGGGGACACC CAAGACAGTG AAAGGGGTCA TCATCCAGGG AGCCCGAGGA GGAGACAGCA    2100
TCACTGCCGT GGAAGCCAGG GCGTTTGTAC GCAAGTTCAA AGTCTCCTAC AGCCTAAATG    2160
GCAAGGACTG GGAATATATC CAGGACCCCA GGACTCAGCA GACAAAGCTG TTTGAAGGGA    2220
ACATGCACTA TGACACCCCT GACATCCGAA GGTTCGATCC TGTTCCAGCG CAGTATGTGC    2280
GGGTGTACCC AGAGAGGTGG TCGCCAGCAG GCATCGGGAT GAGGCTGGAG GTGCTGGGCT    2340
GTGACTGGAC AGACTCAAAG CCCACAGTGG AGACGCTGGG ACCCACCGTG AAGAGTGAAG    2400
AGACTACCAC CCCATATCCC ATGGATGAGG ATGCCACCGA GTGTGGGGAA AACTGCAGCT    2460
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TTGAGGATGA CAAAGATTTG CAACTTCCTT CAGGATTCAA CTGCAACTTT GATTTTCCGG    2520
AAGAGACCTG TGGTTGGGTG TACGACCATG CCAAGTGGCT CCGGAGCACG TGGATCAGCA    2580
GCGCTAACCC CAATGACAGA ACATTTCCAG ATGACAAGAA CTTCTTGAAA CTGCAGAGTG    2640
ATGGCCGACG AGAGGGCCAG TACGGGCGGC TCATCAGCCC ACCGGTGCAC CTGCCCCGAA    2700
GCCCTGTGTG CATGGAGTTC CAGTACCAAG CCATGGGCGG CCACGGGGTG GCACTGCAGG    2760
TGGTTCGGGA AGCCAGCCAG GAAAGCAAAC TCCTTTGGGT CATCCGTGAG GACCAGGGCA    2820
GCGAGTGGAA GCACGGGCGC ATTATCCTGC CCAGCTATGA CATGGAGTAT CAGATCGTGT    2880
TCGAGGGAGT GATAGGGAAG GGACGATCGG GAGAGATTTC CGGCGATGAC ATTCGGATAA    2940
GCACTGATGT CCCACTGGAG AACTGCATGG AACCCATATC AGCTTTTGCA GGTGAGGATT    3000
TTAAAGTGGA CATCCCAGAA ACCCATGGGG GAGAGGGCTA TGAAGATGAG ATTGATGATG    3060
AATATGAAGG AGATTGGAGC AACTCTTCTT CCTCTACCTC AGGGGCTGGT GACCCCTCAT    3120
CTGGCAAAGA AAAGAGCTGG CTGTACACCC TAGATCCCAT TCTGATCACC ATCATCGCCA    3180
TGAGCTCGCT GGGGGTCCTG CTGGGGGCCA CCTGTGCGGG CCTCCTCCTT TACTGCACCT    3240
GCTCCTATTC GGGTCTGAGT TCGAGGAGCT GCACCACACT GGAGAACTAC AACTTTGAGC    3300
TCTACGATGG CCTCAAGCAC AAGGTCAAGA TCAATCATCA GAAGTGCTGC TCGGAGGCAT    3360
GACCGATTGT GTCTGGATCG CTTCTGGCGT TTCATTCCAG TGAGAGGGGC TAGCGAAGAT    3420
TACAGTTTTG TTTTGTTTTG TTTTGTTTTC CCTTTGGAAA CTGAATGCCA TAATCTGGAT    3480
CAAAGTGTTC CAGAATACTG AAGGTATGGA CAGGACAGAC AGGCCAGTCT AGGGAGAAAG    3540
GGAGATGCAG CTGTGAAGGG GATCGTTGCC CACCAGGACT GTGGTGGCCA AGTGAATGCA    3600
GGAACCGGGC CCGGAATTCC GGCTCTCGGC TAAAATCTCA GCTGCCTCTG GAAAGGCTCA    3660
ACCATACTCA GTGCCAACTC AGACTCTGTT GCTGTGGTGT CAACATGGAT GGATCATCTG    3720
TACCTTGTAT TTTTAGCAGA ATTCATGCTC AGATTTCTTT GTTCTGAATC CTTGCTTTGT    3780
GCTAGACACA AAGCATACAT GTCCTTCTAA AATTAATATG ATCACTATAA TCTCCTGTGT    3840
GCAGAATTCA GAAATAGACC TTTGAAACCA TTTGCATTGT GAGTGCAGAT CCATGACTGG    3900
GGCTAGTGCA GCAATGAAAC AGAATTCCAG AAACAGTGTG TTCTTTTTAT TATGGGAAAA    3960
TACAGATAAA AATGGCCACT GATGAACATG AAAGTTAGCA CTTTCCCAAC ACAGTGTACA    4020
CTTGCAACCT TGTTTTGGAT TTCTCATACA CCAAGACTGT GAAACACAAA TTTCAAGAAT    4080
GTGTTCAAAT GTGTGTGTGT GTGTGTGTGT GTGTGTGTGT GTGTGTGTAT GTGTGTGTGT    4140
GTGTGTGTGC TTGTGTGTTT CTGTCAGTGG TATGAGTGAT ATGTATGCAT GTGTGTATGT    4200
ATATGTATGT ATGTATGTAT GTATGTACGT ACATATGTAT GTATGTATGT ATGTATGTAT    4260
GTATGTATAT GTGTGTGTGT GTTTGTGTGT GTGTGTGTTT GTGTGTGTGT GTGTGGTAAG    4320
TGTGGTATGT GTGTATGCAT TTGTCTATAT GTGTATCTGT GTGTCTATGT GTTTCTGTCA    4380
GTGGAATGAG TGGCATGTGT GCATGTGTAT GTATGTGGAT ATGTGTGTTG TGTTTATGTG    4440
CTTGTGTATA AGAGGTAAGT GTGGTGTGTG TGCATGTGTC TCTGTGTGTG TTTGTCTGTG    4500
TACCTCTTTG TATAAGTACC TGTGTTTGTA TGTGGGAATA TGTATATTGA GGCATTGCTG    4560
TGTTAGTATG TTTATAGAAA AGAAGACAGT CTGAGATGTC TTCCTCAATA CCTCTCCACT    4620
TATATCTTGG ATAGACAAAA GTAATGACAA AAAATTGCTG GTGTGTATAT GGAAAAGGGG    4680
GACACATATC CATGGATGGT AGAAGTGTAA ACTGTGCAGT CACTGTGGAC ATCAATATGC    4740
AGGTTCTTCA CAAATGTAGA TATAAAGCTA CTATAGTTAT ACCC                      4784
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(2) INFORMATION FOR SEQ ID NO:16:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 931 amino acids

(B) TYPE: amino acid

(C) STRANDEDNESS: single

(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:16:

```
Met Asp Met Phe Pro Leu Thr Trp Val Phe Leu Ala Leu Tyr Phe Ser
1               5                  10                  15
Gly His Glu Val Arg Ser Gln Gln Asp Pro Pro Cys Gly Gly Arg Pro
            20                  25                  30
Asn Ser Lys Asp Ala Gly Tyr Ile Thr Ser Pro Gly Tyr Pro Gln Asp
        35                  40                  45
Tyr Pro Ser His Gln Asn Cys Glu Trp Ile Val Tyr Ala Pro Glu Pro
    50                  55                  60
Asn Gln Lys Ile Val Leu Asn Phe Asn Pro His Phe Glu Ile Glu Lys
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65                  70                  75                  80
His Asp Cys Lys Tyr Asp Phe Ile Glu Ile Arg Asp Gly Asp Ser Glu
                85                  90                  95
Ser Ala Asp Leu Leu Gly Lys His Cys Gly Asn Ile Ala Pro Pro Thr
            100                 105                 110
Ile Ile Ser Ser Gly Ser Val Leu Tyr Ile Lys Phe Thr Ser Asp Tyr
        115                 120                 125
Ala Arg Gln Gly Ala Gly Phe Ser Leu Arg Tyr Glu Ile Phe Lys Thr
    130                 135                 140
Gly Ser Glu Asp Cys Ser Lys Asn Phe Thr Ser Pro Asn Gly Thr Ile
145                 150                 155                 160
Glu Ser Pro Gly Phe Pro Glu Lys Tyr Pro His Asn Leu Asp Cys Thr
                165                 170                 175
Phe Thr Ile Leu Ala Lys Pro Arg Met Glu Ile Ile Leu Gln Phe Leu
            180                 185                 190
Thr Phe Asp Leu Glu His Asp Pro Leu Gln Val Gly Glu Gly Asp Cys
        195                 200                 205
Lys Tyr Asp Trp Leu Asp Ile Trp Asp Gly Ile Pro His Val Gly Pro
    210                 215                 220
Leu Ile Gly Lys Tyr Cys Gly Thr Lys Thr Pro Ser Lys Leu Arg Ser
225                 230                 235                 240
Ser Thr Gly Ile Leu Ser Leu Thr Phe His Thr Asp Met Ala Val Ala
                245                 250                 255
Lys Asp Gly Phe Ser Ala Arg Tyr Tyr Leu Ile His Gln Glu Pro Pro
            260                 265                 270
Glu Asn Phe Gln Cys Asn Val Pro Leu Gly Met Glu Ser Gly Arg Ile
        275                 280                 285
Ala Asn Glu Gln Ile Ser Ala Ser Ser Thr Phe Ser Asp Gly Arg Trp
    290                 295                 300
Thr Pro Gln Gln Ser Arg Leu His Gly Asp Asp Asn Gly Trp Thr Pro
305                 310                 315                 320
Asn Leu Asp Ser Asn Lys Glu Tyr Leu Gln Val Asp Leu Arg Phe Leu
                325                 330                 335
Thr Met Leu Thr Ala Ile Ala Thr Gln Gly Ala Ile Ser Arg Glu Thr
            340                 345                 350
Gln Lys Gly Tyr Tyr Val Lys Ser Tyr Lys Leu Glu Val Ser Thr Asn
        355                 360                 365
Gly Glu Asp Trp Met Val Tyr Arg His Gly Lys Asn His Lys Ile Phe
    370                 375                 380
Gln Ala Asn Asn Asp Ala Thr Glu Val Val Leu Asn Lys Leu His Met
385                 390                 395                 400
Pro Leu Leu Thr Arg Phe Ile Arg Ile Arg Pro Gln Thr Trp His Leu
                405                 410                 415
Gly Ile Ala Leu Arg Leu Glu Leu Phe Gly Cys Arg Val Thr Asp Ala
            420                 425                 430
Pro Cys Ser Asn Met Leu Gly Met Leu Ser Gly Leu Ile Ala Asp Thr
        435                 440                 445
Gln Ile Ser Ala Ser Ser Thr Arg Glu Tyr Leu Trp Ser Pro Ser Ala
    450                 455                 460
Ala Arg Leu Val Ser Ser Arg Ser Gly Trp Phe Pro Arg Asn Pro Gln
465                 470                 475                 480
Ala Gln Pro Gly Glu Glu Trp Leu Gln Val Asp Leu Gly Thr Pro Lys
                485                 490                 495
Thr Val Lys Gly Val Ile Ile Gln Gly Ala Arg Gly Gly Asp Ser Ile
            500                 505                 510
Thr Ala Val Glu Ala Arg Ala Phe Val Arg Lys Phe Lys Val Ser Tyr
        515                 520                 525
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Ser Leu Asn Gly Lys Asp Trp Glu Tyr Ile Gln Asp Pro Arg Thr Gln
    530                 535                 540
Gln Thr Lys Leu Phe Glu Gly Asn Met His Tyr Asp Thr Pro Asp Ile
545                 550                 555                 560
Arg Arg Phe Asp Pro Val Pro Ala Gln Tyr Val Arg Val Tyr Pro Glu
                565                 570                 575
Arg Trp Ser Pro Ala Gly Ile Gly Met Arg Leu Glu Val Leu Gly Cys
            580                 585                 590
Asp Trp Thr Asp Ser Lys Pro Thr Val Glu Thr Leu Gly Pro Thr Val
        595                 600                 605
Lys Ser Glu Glu Thr Thr Thr Pro Tyr Pro Met Asp Glu Asp Ala Thr
    610                 615                 620
Glu Cys Gly Glu Asn Cys Ser Phe Glu Asp Asp Lys Asp Leu Gln Leu
625                 630                 635                 640
Pro Ser Gly Phe Asn Cys Asn Phe Asp Phe Pro Glu Glu Thr Cys Gly
                645                 650                 655
Trp Val Tyr Asp His Ala Lys Trp Leu Arg Ser Thr Trp Ile Ser Ser
            660                 665                 670
Ala Asn Pro Asn Asp Arg Thr Phe Pro Asp Asp Lys Asn Phe Leu Lys
        675                 680                 685
Leu Gln Ser Asp Gly Arg Arg Glu Gly Gln Tyr Gly Arg Leu Ile Ser
    690                 695                 700
Pro Pro Val His Leu Pro Arg Ser Pro Val Cys Met Glu Phe Gln Tyr
705                 710                 715                 720
Gln Ala Met Gly Gly His Gly Val Ala Leu Gln Val Val Arg Glu Ala
                725                 730                 735
Ser Gln Glu Ser Lys Leu Leu Trp Val Ile Arg Glu Asp Gln Gly Ser
            740                 745                 750
Glu Trp Lys His Gly Arg Ile Ile Leu Pro Ser Tyr Asp Met Glu Tyr
        755                 760                 765
Gln Ile Val Phe Glu Gly Val Ile Gly Lys Gly Arg Ser Gly Glu Ile
    770                 775                 780
Ser Gly Asp Asp Ile Arg Ile Ser Thr Asp Val Pro Leu Glu Asn Cys
785                 790                 795                 800
Met Glu Pro Ile Ser Ala Phe Ala Gly Glu Asp Phe Lys Val Asp Ile
                805                 810                 815
Pro Glu Thr His Gly Gly Glu Gly Tyr Glu Asp Glu Ile Asp Asp Glu
            820                 825                 830
Tyr Glu Gly Asp Trp Ser Asn Ser Ser Ser Ser Thr Ser Gly Ala Gly
        835                 840                 845
Asp Pro Ser Ser Gly Lys Glu Lys Ser Trp Leu Tyr Thr Leu Asp Pro
    850                 855                 860
Ile Leu Ile Thr Ile Ile Ala Met Ser Ser Leu Gly Val Leu Leu Gly
865                 870                 875                 880
Ala Thr Cys Ala Gly Leu Leu Leu Tyr Cys Thr Cys Ser Tyr Ser Gly
                885                 890                 895
Leu Ser Ser Arg Ser Cys Thr Thr Leu Glu Asn Tyr Asn Phe Glu Leu
            900                 905                 910
Tyr Asp Gly Leu Lys His Lys Val Lys Ile Asn His Gln Lys Cys Cys
        915                 920                 925
Ser Glu Ala
    930
```

(2) INFORMATION FOR SEQ ID NO:17:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 2730 base pairs

(B) TYPE: nucleic acid

human SR2(a)0

(C) STRANDEDNESS: double
(D) TOPOLOGY: linear
(ii) MOLECULE TYPE: cDNA
(xi) SEQUENCE DESCRIPTION: SEQ ID NO:17:

ATGGATATGT TTCCTCTCAC CTGGGTTTTC TTAGCCCTCT ACTTTTCAAG ACACCAAGTG 60
AGAGGCCAAC CAGACCCACC GTGCGGAGGT CGTTTGAATT CCAAAGATGC TGGCTATATC 120
ACCTCTCCCG GTTACCCCCA GGACTACCCC TCCCACCAGA ACTGCGAGTG GATTGTTTAC 180
GCCCCCGAAC CCAACCAGAA GATTGTCCTC AACTTCAACC CTCACTTTGA AATCGAGAAG 240
CACGACTGCA AGTATGACTT TATCGAGATT CGGGATGGGG ACAGTGAATC CGCAGACCTC 300
CTGGGCAAAC ACTGTGGGAA CATCGCCCCG CCCACCATCA TCTCCTCGGG CTCCATGCTC 360
TACATCAAGT TCACCTCCGA CTACGCCCGG CAGGGGGCAG GCTTCTCTCT GCGCTACGAG 420
ATCTTCAAGA CAGGCTCTGA AGATTGCTCA AAAAACTTCA CAAGCCCCAA CGGGACCATC 480
GAATCTCCTG GGTTTCCTGA GAAGTATCCA CACAACTTGG ACTGCACCTT TACCATCCTG 540
GCCAAACCCA AGATGGAGAT CATCCTGCAG TTCCTGATCT TTGACCTGGA GCATGACCCT 600
TTGCAGGTGG GAGAGGGGGA CTGCAAGTAC GATTGGCTGG ACATCTGGGA TGGCATTCCA 660
CATGTTGGCC CCCTGATTGG CAAGTACTGT GGGACCAAAA CACCCTCTGA ACTTCGTTCA 720
TCGACGGGGA TCCTCTCCCT GACCTTTCAC ACGGACATGG CGGTGGCCAA GGATGGCTTC 780
TCTGCGCGTT ACTACCTGGT CCACCAAGAG CCACTAGAGA ACTTTCAGTG CAATGTTCCT 840
CTGGGCATGG AGTCTGGCCG GATTGCTAAT GAACAGATCA GTGCCTCATC TACCTACTCT 900
GATGGGAGGT GGACCCCTCA ACAAAGCCGG CTCCATGGTG ATGACAATGG CTGGACCCCC 960
AACTTGGATT CCAACAAGGA GTATCTCCAG GTGGACCTGC GCTTTTTAAC CATGCTCACG 1020
GCCATCGCAA CACAGGGAGC GATTTCCAGG GAAACACAGA ATGGCTACTA CGTCAAATCC 1080
TACAAGCTGG AAGTCAGCAC TAATGGAGAG GACTGGATGG TGTACCGGCA TGGCAAAAAC 1140
CACAAGGTAT TTCAAGCCAA CAACGATGCA ACTGAGGTGG TTCTGAACAA GCTCCACGCT 1200
CCACTGCTGA CAAGGTTTGT TAGAATCCGC CCTCAGACCT GGCACTCAGG TATCGCCCTC 1260
CGGCTGGAGC TCTTCGGCTG CCGGGTCACA GATGCTCCCT GCTCCAACAT GCTGGGGATG 1320
CTCTCAGGCC TCATTGCAGA CTCCCAGATC TCCGCCTCTT CCACCCAGGA ATACCTCTGG 1380
AGCCCCAGTG CAGCCCGCCT GGTCAGCAGC CGCTCGGGCT GGTTCCCTCG AATCCCTCAG 1440
GCCCAGCCCG GTGAGGAGTG GCTTCAGGTA GATCTGGGAA CACCCAAGAC AGTGAAAGGT 1500
GTCATCATCC AGGGAGCCCG CGGAGGAGAC AGTATCACTG CTGTGGAAGC CAGAGCATTT 1560
GTGCGCAAGT TCAAAGTCTC CTACAGCCTA AACGGCAAGG ACTGGGAATA CATTCAGGAC 1620
CCCAGGACCC AGCAGCCAAA GCTGTTCGAA GGGAACATGC ACTATGACAC CCCTGACATC 1680
CGAAGGTTTG ACCCCATTCC GGCACAGTAT GTGCGGGTAT ACCCGGAGAG GTGGTCGCCG 1740
GCGGGGATTG GGATGCGGCT GGAGGTGCTG GGCTGTGACT GGACAGACTC CAAGCCCACG 1800
GTAAAAACGC TGGGACCCAC TGTGAAGAGC GAAGAGACAA CCACCCCCTA CCCCACCGAA 1860
GAGGAGGCCA CAGAGTGTGG GGAGAACTGC AGCTTTGAGG ATGACAAAGA TTTGCAGCTC 1920
CCTTCGGGAT TCAATTGCAA CTTCGATTTC CTCGAGGAGC CCTGTGGTTG GATGTATGAC 1980
CATGCCAAGT GGCTCCGGAC CACCTGGGCC AGCAGCTCCA GCCCAAACGA CCGGACGTTT 2040
CCAGATGACA GGAATTTCTT GCGGCTGCAG AGTGACAGCC AGAGAGAGGG CCAGTATGCC 2100
CGGCTCATCA GCCCCCCTGT CCACCTGCCC CGAAGCCCGG TGTGCATGGA GTTCCAGTAC 2160
CAGGCCACGG GCGGCCGCGG GGTGGCGCTG CAGGTGGTGC GGGAAGCCAG CCAGGAGAGC 2220
AAGTTGCTGT GGGTCATCCG TGAGGACCAG GGCGGCGAGT GGAAGCACGG GCGGATCATC 2280
CTGCCCAGCT ACGACATGGA GTACCAGATT GTGTTCGAGG GAGTGATAGG GAAAGGACGT 2340
TCCGGAGAGA TTGCCATTGA TGACATTCGG ATAAGCACTG ATGTCCCACT GGAGAACTGC 2400
ATGGAACCCA TCTCGGCTTT TGCAGATGAA TACGAGGTGG ACTGGAGCAA TTCTTCTTCT 2460
GCAACCTCAG GGTCTGGCGC CCCCTCGACC GACAAAGAAA AGAGCTGGCT GTACACCCTG 2520
GATCCCATCC TCATCACCAT CATCGCCATG AGCTCACTGG GCGTCCTCCT GGGGGCCACC 2580
TGTGCAGGCC TCCTGCTCTA CTGCACCTGT TCCTACTCGG GCCTGAGCTC CCGAAGCTGC 2640
ACCACACTGG AGAACTACAA CTTCGAGCTC TACGATGGCC TTAAGCACAA GGTCAAGATG 2700
AACCACCAAA AGTGCTGCTC CGAGGCATGA 2730

(2) INFORMATION FOR SEQ ID NO:18:
(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 909 amino acids
(B) TYPE: amino acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide
(xi) SEQUENCE DESCRIPTION: SEQ ID NO:18:

```
Met Asp Met Phe Pro Leu Thr Trp Val Phe Leu Ala Leu Tyr Phe Ser
1               5                  10                  15
Arg His Gln Val Arg Gly Gln Pro Asp Pro Pro Cys Gly Gly Arg Leu
            20                  25                  30
Asn Ser Lys Asp Ala Gly Tyr Ile Thr Ser Pro Gly Tyr Pro Gln Asp
        35                  40                  45
Tyr Pro Ser His Gln Asn Cys Glu Trp Ile Val Tyr Ala Pro Glu Pro
    50                  55                  60
Asn Gln Lys Ile Val Leu Asn Phe Asn Pro His Phe Glu Ile Glu Lys
65                  70                  75                  80
His Asp Cys Lys Tyr Asp Phe Ile Glu Ile Arg Asp Gly Asp Ser Glu
                85                  90                  95
Ser Ala Asp Leu Leu Gly Lys His Cys Gly Asn Ile Ala Pro Pro Thr
            100                 105                 110
Ile Ile Ser Ser Gly Ser Met Leu Tyr Ile Lys Phe Thr Ser Asp Tyr
        115                 120                 125
Ala Arg Gln Gly Ala Gly Phe Ser Leu Arg Tyr Glu Ile Phe Lys Thr
    130                 135                 140
Gly Ser Glu Asp Cys Ser Lys Asn Phe Thr Ser Pro Asn Gly Thr Ile
145                 150                 155                 160
Glu Ser Pro Gly Phe Pro Glu Lys Tyr Pro His Asn Leu Asp Cys Thr
                165                 170                 175
Phe Thr Ile Leu Ala Lys Pro Lys Met Glu Ile Ile Leu Gln Phe Leu
            180                 185                 190
Ile Phe Asp Leu Glu His Asp Pro Leu Gln Val Gly Glu Gly Asp Cys
        195                 200                 205
Lys Tyr Asp Trp Leu Asp Ile Trp Asp Gly Ile Pro His Val Gly Pro
    210                 215                 220
Leu Ile Gly Lys Tyr Cys Gly Thr Lys Thr Pro Ser Glu Leu Arg Ser
225                 230                 235                 240
Ser Thr Gly Ile Leu Ser Leu Thr Phe His Thr Asp Met Ala Val Ala
                245                 250                 255
Lys Asp Gly Phe Ser Ala Arg Tyr Tyr Leu Val His Gln Glu Pro Leu
            260                 265                 270
Glu Asn Phe Gln Cys Asn Val Pro Leu Gly Met Glu Ser Gly Arg Ile
        275                 280                 285
Ala Asn Glu Gln Ile Ser Ala Ser Ser Thr Tyr Ser Asp Gly Arg Trp
    290                 295                 300
Thr Pro Gln Gln Ser Arg Leu His Gly Asp Asp Asn Gly Trp Thr Pro
305                 310                 315                 320
Asn Leu Asp Ser Asn Lys Glu Tyr Leu Gln Val Asp Leu Arg Phe Leu
                325                 330                 335
Thr Met Leu Thr Ala Ile Ala Thr Gln Gly Ala Ile Ser Arg Glu Thr
            340                 345                 350
Gln Asn Gly Tyr Tyr Val Lys Ser Tyr Lys Leu Glu Val Ser Thr Asn
        355                 360                 365
Gly Glu Asp Trp Met Val Tyr Arg His Gly Lys Asn His Lys Val Phe
    370                 375                 380
Gln Ala Asn Asn Asp Ala Thr Glu Val Val Leu Asn Lys Leu His Ala
385                 390                 395                 400
Pro Leu Leu Thr Arg Phe Val Arg Ile Arg Pro Gln Thr Trp His Ser
                405                 410                 415
Gly Ile Ala Leu Arg Leu Glu Leu Phe Gly Cys Arg Val Thr Asp Ala
            420                 425                 430
Pro Cys Ser Asn Met Leu Gly Met Leu Ser Gly Leu Ile Ala Asp Ser
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        435                 440                 445
Gln Ile Ser Ala Ser Ser Thr Gln Glu Tyr Leu Trp Ser Pro Ser Ala
    450                 455                 460
Ala Arg Leu Val Ser Ser Arg Ser Gly Trp Phe Pro Arg Ile Pro Gln
465                 470                 475                 480
Ala Gln Pro Gly Glu Glu Trp Leu Gln Val Asp Leu Gly Thr Pro Lys
                485                 490                 495
Thr Val Lys Gly Val Ile Ile Gln Gly Ala Arg Gly Gly Asp Ser Ile
            500                 505                 510
Thr Ala Val Glu Ala Arg Ala Phe Val Arg Lys Phe Lys Val Ser Tyr
        515                 520                 525
Ser Leu Asn Gly Lys Asp Trp Glu Tyr Ile Gln Asp Pro Arg Thr Gln
    530                 535                 540
Gln Pro Lys Leu Phe Glu Gly Asn Met His Tyr Asp Thr Pro Asp Ile
545                 550                 555                 560
Arg Arg Phe Asp Pro Ile Pro Ala Gln Tyr Val Arg Val Tyr Pro Glu
                565                 570                 575
Arg Trp Ser Pro Ala Gly Ile Gly Met Arg Leu Glu Val Leu Gly Cys
            580                 585                 590
Asp Trp Thr Asp Ser Lys Pro Thr Val Lys Thr Leu Gly Pro Thr Val
        595                 600                 605
Lys Ser Glu Glu Thr Thr Thr Pro Tyr Pro Thr Glu Glu Glu Ala Thr
    610                 615                 620
Glu Cys Gly Glu Asn Cys Ser Phe Glu Asp Asp Lys Asp Leu Gln Leu
625                 630                 635                 640
Pro Ser Gly Phe Asn Cys Asn Phe Asp Phe Leu Glu Glu Pro Cys Gly
                645                 650                 655
Trp Met Tyr Asp His Ala Lys Trp Leu Arg Thr Thr Trp Ala Ser Ser
            660                 665                 670
Ser Ser Pro Asn Asp Arg Thr Phe Pro Asp Asp Arg Asn Phe Leu Arg
        675                 680                 685
Leu Gln Ser Asp Ser Gln Arg Glu Gly Gln Tyr Ala Arg Leu Ile Ser
    690                 695                 700
Pro Pro Val His Leu Pro Arg Ser Pro Val Cys Met Glu Phe Gln Tyr
705                 710                 715                 720
Gln Ala Thr Gly Gly Arg Gly Val Ala Leu Gln Val Val Arg Glu Ala
                725                 730                 735
Ser Gln Glu Ser Lys Leu Leu Trp Val Ile Arg Glu Asp Gln Gly Gly
            740                 745                 750
Glu Trp Lys His Gly Arg Ile Ile Leu Pro Ser Tyr Asp Met Glu Tyr
        755                 760                 765
Gln Ile Val Phe Glu Gly Val Ile Gly Lys Gly Arg Ser Gly Glu Ile
    770                 775                 780
Ala Ile Asp Asp Ile Arg Ile Ser Thr Asp Val Pro Leu Glu Asn Cys
785                 790                 795                 800
Met Glu Pro Ile Ser Ala Phe Ala Asp Glu Tyr Glu Val Asp Trp Ser
                805                 810                 815
Asn Ser Ser Ser Ala Thr Ser Gly Ser Gly Ala Pro Ser Thr Asp Lys
            820                 825                 830
Glu Lys Ser Trp Leu Tyr Thr Leu Asp Pro Ile Leu Ile Thr Ile Ile
        835                 840                 845
Ala Met Ser Ser Leu Gly Val Leu Leu Gly Ala Thr Cys Ala Gly Leu
    850                 855                 860
Leu Leu Tyr Cys Thr Cys Ser Tyr Ser Gly Leu Ser Ser Arg Ser Cys
865                 870                 875                 880
Thr Thr Leu Glu Asn Tyr Asn Phe Glu Leu Tyr Asp Gly Leu Lys His
                885                 890                 895
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Lys Val Lys Met Asn His Gln Lys Cys Cys Ser Glu Ala
900 905

human SR2(b)17

(2) INFORMATION FOR SEQ ID NO:19:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 2781 base pairs

(B) TYPE: nucleic acid

(C) STRANDEDNESS: single

(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: cDNA

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:19:

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ATGGATATGT TTCCTCTCAC CTGGGTTTTC TTAGCCCTCT ACTTTTCAAG ACACCAAGTG      60
AGAGGCCAAC CAGACCCACC GTGCGGAGGT CGTTTGAATT CCAAAGATGC TGGCTATATC     120
ACCTCTCCCG GTTACCCCCA GGACTACCCC TCCCACCAGA ACTGCGAGTG GATTGTTTAC     180
GCCCCCGAAC CCAACCAGAA GATTGTCCTC AACTTCAACC CTCACTTTGA AATCGAGAAG     240
CACGACTGCA AGTATGACTT TATCGAGATT CGGGATGGGG ACAGTGAATC CGCAGACCTC     300
CTGGGCAAAC ACTGTGGGAA CATCGCCCCG CCCACCATCA TCTCCTCGGG CTCCATGCTC     360
TACATCAAGT TCACCTCCGA CTACGCCCGG CAGGGGGCAG GCTTCTCTCT GCGCTACGAG     420
ATCTTCAAGA CAGGCTCTGA AGATTGCTCA AAAAACTTCA CAAGCCCCAA CGGGACCATC     480
GAATCTCCTG GGTTTCCTGA GAAGTATCCA CACAACTTGG ACTGCACCTT TACCATCCTG     540
GCCAAACCCA AGATGGAGAT CATCCTGCAG TTCCTGATCT TTGACCTGGA GCATGACCCT     600
TTGCAGGTGG GAGAGGGGGA CTGCAAGTAC GATTGGCTGG ACATCTGGGA TGGCATTCCA     660
CATGTTGGCC CCCTGATTGG CAAGTACTGT GGGACCAAAA CACCCTCTGA ACTTCGTTCA     720
TCGACGGGGA TCCTCTCCCT GACCTTTCAC ACGGACATGG CGGTGGCCAA GGATGGCTTC     780
TCTGCGCGTT ACTACCTGGT CCACCAAGAG CCACTAGAGA ACTTTCAGTG CAATGTTCCT     840
CTGGGCATGG AGTCTGGCCG GATTGCTAAT GAACAGATCA GTGCCTCATC TACCTACTCT     900
GATGGGAGGT GGACCCCTCA ACAAAGCCGG CTCCATGGTG ATGACAATGG CTGGACCCCC     960
AACTTGGATT CCAACAAGGA GTATCTCCAG GTGGACCTGC GCTTTTTAAC CATGCTCACG    1020
GCCATCGCAA CACAGGGAGC GATTTCCAGG GAAACACAGA ATGGCTACTA CGTCAAATCC    1080
TACAAGCTGG AAGTCAGCAC TAATGGAGAG GACTGGATGG TGTACCGGCA TGGCAAAAAC    1140
CACAAGGTAT TTCAAGCCAA CAACGATGCA ACTGAGGTGG TTCTGAACAA GCTCCACGCT    1200
CCACTGCTGA CAAGGTTTGT TAGAATCCGC CCTCAGACCT GGCACTCAGG TATCGCCCTC    1260
CGGCTGGAGC TCTTCGGCTG CCGGGTCACA GATGCTCCCT GCTCCAACAT GCTGGGGATG    1320
CTCTCAGGCC TCATTGCAGA CTCCCAGATC TCCGCCTCTT CCACCCAGGA ATACCTCTGG    1380
AGCCCCAGTG CAGCCCGCCT GGTCAGCAGC CGCTCGGGCT GGTTCCCTCG AATCCCTCAG    1440
GCCCAGCCCG GTGAGGAGTG GCTTCAGGTA GATCTGGGAA CACCCAAGAC AGTGAAAGGT    1500
GTCATCATCC AGGGAGCCCG CGGAGGAGAC AGTATCACTG CTGTGGAAGC CAGAGCATTT    1560
GTGCGCAAGT TCAAAGTCTC CTACAGCCTA AACGGCAAGG ACTGGGAATA CATTCAGGAC    1620
CCCAGGACCC AGCAGCCAAA GCTGTTCGAA GGGAACATGC ACTATGACAC CCCTGACATC    1680
CGAAGGTTTG ACCCCATTCC GGCACAGTAT GTGCGGGTAT ACCCGGAGAG GTGGTCGCCG    1740
GCGGGGATTG GGATGCGGCT GGAGGTGCTG GGCTGTGACT GGACAGACTC CAAGCCCACG    1800
GTAAAAACGC TGGGACCCAC TGTGAAGAGC GAAGAGACAA CCACCCCCTA CCCCACCGAA    1860
GAGGAGGCCA CAGAGTGTGG GGAGAACTGC AGCTTTGAGG ATGACAAAGA TTTGCAGCTC    1920
CCTTCGGGAT TCAATTGCAA CTTCGATTTC CTCGAGGAGC CCTGTGGTTG GATGTATGAC    1980
CATGCCAAGT GGCTCCGGAC CACCTGGGCC AGCAGCTCCA GCCCAAACGA CCGGACGTTT    2040
CCAGATGACA GGAATTTCTT GCGGCTGCAG AGTGACAGCC AGAGAGAGGG CCAGTATGCC    2100
CGGCTCATCA GCCCCCCTGT CCACCTGCCC CGAAGCCCGG TGTGCATGGA GTTCCAGTAC    2160
CAGGCCACGG GCGGCCGCGG GGTGGCGCTG CAGGTGGTGC GGGAAGCCAG CCAGGAGAGC    2220
AAGTTGCTGT GGGTCATCCG TGAGGACCAG GGCGGCGAGT GGAAGCACGG GCGGATCATC    2280
CTGCCCAGCT ACGACATGGA GTACCAGATT GTGTTCGAGG GAGTGATAGG GAAAGGACGT    2340
TCCGGAGAGA TTGCCATTGA TGACATTCGG ATAAGCACTG ATGTCCCACT GGAGAACTGC    2400
ATGGAACCCA TCTCGGCTTT TGCAGTGGAC ATCCCAGAAA TACATGAGAG AGAAGGATAT    2460
GAAGATGAAA TTGATGATGA ATACGAGGTG GACTGGAGCA ATTCTTCTTC TGCAACCTCA    2520
GGGTCTGGCG CCCCCTCGAC CGACAAAGAA AAGAGCTGGC TGTACACCCT GGATCCCATC    2580
CTCATCACCA TCATCGCCAT GAGCTCACTG GGCGTCCTCC TGGGGGCCAC CTGTGCAGGC    2640
CTCCTGCTCT ACTGCACCTG TTCCTACTCG GGCCTGAGCT CCCGAAGCTG CACCACACTG    2700
GAGAACTACA ACTTCGAGCT CTACGATGGC CTTAAGCACA AGGTCAAGAT GAACCACCAA    2760
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AAGTGCTGCT CCGAGGCATG A 2781

(2) INFORMATION FOR SEQ ID NO:20:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 926 amino acids

(B) TYPE: amino acid

(C) STRANDEDNESS: single

(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:20:

```
Met Asp Met Phe Pro Leu Thr Trp Val Phe Leu Ala Leu Tyr Phe Ser
1               5                  10                  15
Arg His Gln Val Arg Gly Gln Pro Asp Pro Pro Cys Gly Gly Arg Leu
            20                  25                  30
Asn Ser Lys Asp Ala Gly Tyr Ile Thr Ser Pro Gly Tyr Pro Gln Asp
        35                  40                  45
Tyr Pro Ser His Gln Asn Cys Glu Trp Ile Val Tyr Ala Pro Glu Pro
    50                  55                  60
Asn Gln Lys Ile Val Leu Asn Phe Asn Pro His Phe Glu Ile Glu Lys
65                  70                  75                  80
His Asp Cys Lys Tyr Asp Phe Ile Glu Ile Arg Asp Gly Asp Ser Glu
                85                  90                  95
Ser Ala Asp Leu Leu Gly Lys His Cys Gly Asn Ile Ala Pro Pro Thr
            100                 105                 110
Ile Ile Ser Ser Gly Ser Met Leu Tyr Ile Lys Phe Thr Ser Asp Tyr
        115                 120                 125
Ala Arg Gln Gly Ala Gly Phe Ser Leu Arg Tyr Glu Ile Phe Lys Thr
    130                 135                 140
Gly Ser Glu Asp Cys Ser Lys Asn Phe Thr Ser Pro Asn Gly Thr Ile
145                 150                 155                 160
Glu Ser Pro Gly Phe Pro Glu Lys Tyr Pro His Asn Leu Asp Cys Thr
                165                 170                 175
Phe Thr Ile Leu Ala Lys Pro Lys Met Glu Ile Ile Leu Gln Phe Leu
            180                 185                 190
Ile Phe Asp Leu Glu His Asp Pro Leu Gln Val Gly Glu Gly Asp Cys
        195                 200                 205
Lys Tyr Asp Trp Leu Asp Ile Trp Asp Gly Ile Pro His Val Gly Pro
    210                 215                 220
Leu Ile Gly Lys Tyr Cys Gly Thr Lys Thr Pro Ser Glu Leu Arg Ser
225                 230                 235                 240
Ser Thr Gly Ile Leu Ser Leu Thr Phe His Thr Asp Met Ala Val Ala
                245                 250                 255
Lys Asp Gly Phe Ser Ala Arg Tyr Tyr Leu Val His Gln Glu Pro Leu
            260                 265                 270
Glu Asn Phe Gln Cys Asn Val Pro Leu Gly Met Glu Ser Gly Arg Ile
        275                 280                 285
Ala Asn Glu Gln Ile Ser Ala Ser Ser Thr Tyr Ser Asp Gly Arg Trp
    290                 295                 300
Thr Pro Gln Gln Ser Arg Leu His Gly Asp Asp Asn Gly Trp Thr Pro
305                 310                 315                 320
Asn Leu Asp Ser Asn Lys Glu Tyr Leu Gln Val Asp Leu Arg Phe Leu
                325                 330                 335
Thr Met Leu Thr Ala Ile Ala Thr Gln Gly Ala Ile Ser Arg Glu Thr
            340                 345                 350
Gln Asn Gly Tyr Tyr Val Lys Ser Tyr Lys Leu Glu Val Ser Thr Asn
        355                 360                 365
Gly Glu Asp Trp Met Val Tyr Arg His Gly Lys Asn His Lys Val Phe
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    370                 375                 380
Gln Ala Asn Asn Asp Ala Thr Glu Val Val Leu Asn Lys Leu His Ala
385                 390                 395                 400
Pro Leu Leu Thr Arg Phe Val Arg Ile Arg Pro Gln Thr Trp His Ser
                405                 410                 415
Gly Ile Ala Leu Arg Leu Glu Leu Phe Gly Cys Arg Val Thr Asp Ala
            420                 425                 430
Pro Cys Ser Asn Met Leu Gly Met Leu Ser Gly Leu Ile Ala Asp Ser
        435                 440                 445
Gln Ile Ser Ala Ser Ser Thr Gln Glu Tyr Leu Trp Ser Pro Ser Ala
    450                 455                 460
Ala Arg Leu Val Ser Ser Arg Ser Gly Trp Phe Pro Arg Ile Pro Gln
465                 470                 475                 480
Ala Gln Pro Gly Glu Glu Trp Leu Gln Val Asp Leu Gly Thr Pro Lys
                485                 490                 495
Thr Val Lys Gly Val Ile Ile Gln Gly Ala Arg Gly Gly Asp Ser Ile
            500                 505                 510
Thr Ala Val Glu Ala Arg Ala Phe Val Arg Lys Phe Lys Val Ser Tyr
        515                 520                 525
Ser Leu Asn Gly Lys Asp Trp Glu Tyr Ile Gln Asp Pro Arg Thr Gln
    530                 535                 540
Gln Pro Lys Leu Phe Glu Gly Asn Met His Tyr Asp Thr Pro Asp Ile
545                 550                 555                 560
Arg Arg Phe Asp Pro Ile Pro Ala Gln Tyr Val Arg Val Tyr Pro Glu
                565                 570                 575
Arg Trp Ser Pro Ala Gly Ile Gly Met Arg Leu Glu Val Leu Gly Cys
            580                 585                 590
Asp Trp Thr Asp Ser Lys Pro Thr Val Lys Thr Leu Gly Pro Thr Val
        595                 600                 605
Lys Ser Glu Glu Thr Thr Thr Pro Tyr Pro Thr Glu Glu Glu Ala Thr
    610                 615                 620
Glu Cys Gly Glu Asn Cys Ser Phe Glu Asp Asp Lys Asp Leu Gln Leu
625                 630                 635                 640
Pro Ser Gly Phe Asn Cys Asn Phe Asp Phe Leu Glu Glu Pro Cys Gly
                645                 650                 655
Trp Met Tyr Asp His Ala Lys Trp Leu Arg Thr Thr Trp Ala Ser Ser
            660                 665                 670
Ser Ser Pro Asn Asp Arg Thr Phe Pro Asp Asp Arg Asn Phe Leu Arg
        675                 680                 685
Leu Gln Ser Asp Ser Gln Arg Glu Gly Gln Tyr Ala Arg Leu Ile Ser
    690                 695                 700
Pro Pro Val His Leu Pro Arg Ser Pro Val Cys Met Glu Phe Gln Tyr
705                 710                 715                 720
Gln Ala Thr Gly Gly Arg Gly Val Ala Leu Gln Val Val Arg Glu Ala
                725                 730                 735
Ser Gln Glu Ser Lys Leu Leu Trp Val Ile Arg Glu Asp Gln Gly Gly
            740                 745                 750
Glu Trp Lys His Gly Arg Ile Ile Leu Pro Ser Tyr Asp Met Glu Tyr
        755                 760                 765
Gln Ile Val Phe Glu Gly Val Ile Gly Lys Gly Arg Ser Gly Glu Ile
    770                 775                 780
Ala Ile Asp Asp Ile Arg Ile Ser Thr Asp Val Pro Leu Glu Asn Cys
785                 790                 795                 800
Met Glu Pro Ile Ser Ala Phe Ala Val Asp Ile Pro Glu Ile His Glu
                805                 810                 815
Arg Glu Gly Tyr Glu Asp Glu Ile Asp Asp Glu Tyr Glu Val Asp Trp
            820                 825                 830
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Ser Asn Ser Ser Ser Ala Thr Ser Gly Ser Gly Ala Pro Ser Thr Asp
        835                 840                 845
Lys Glu Lys Ser Trp Leu Tyr Thr Leu Asp Pro Ile Leu Ile Thr Ile
    850                 855                 860
Ile Ala Met Ser Ser Leu Gly Val Leu Leu Gly Ala Thr Cys Ala Gly
865                 870                 875                 880
Leu Leu Leu Tyr Cys Thr Cys Ser Tyr Ser Gly Leu Ser Ser Arg Ser
                885                 890                 895
Cys Thr Thr Leu Glu Asn Tyr Asn Phe Glu Leu Tyr Asp Gly Leu Lys
            900                 905                 910
His Lys Val Lys Met Asn His Gln Lys Cys Cys Ser Glu Ala
        915                 920                 925
```

more SR2(b)0

(2) INFORMATION FOR SEQ ID NO:21:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 4765 base pairs

(B) TYPE: nucleic acid

(C) STRANDEDNESS: single

(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: cDNA

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:21:

```
AAACTGGAGC TCCACCGCGG TGGCGGCCGC CCGGGCAGGT CTAGAATTCA GCGGCCGCTG      60
AATTCTATCC AGCGGTCGGT GCCTCTGCCC GCGTGTGTGT CCCGGGTGCC GGGGGACCTG     120
TGTCAGTTAG CGCTTCTGAG ATCACACAGC TGCCTAGGGG CCGTGTGATG CCCAGGGCAA     180
TTCTTGGCTT TGATTTTTAT TATTATTACT ATTATTTTGC GTTCAGCTTT CGGGAAACCC     240
TCGTGATGTT GTAGGATAAA GGAAATGACA CTTTGAGGAA CTGGAGAGAA CATACACGCG     300
TTTGGGTTTG AAGAGGAAAC CGGTCTCCGC TTCCTTAGCT TGCTCCCTCT TTGCTGATTT     360
CAAGAGCTAT CTCCTATGAG GTGGAGATAT TCCAGCAAGA ATAAAGGTGA AGACAGACTG     420
ACTGCCAGGA CCCAGGAGGA AAACGTTGAT CGTTAGAGAC CTTTGCAGAA GACACCACCA     480
GGAGGAAAAT TAGAGAGGAA AAACACAAAG ACATAATTAT AGGAGATCCC ACAAACCTAG     540
CCCGGGAGAG AGCCTCTCTG TCAAAAATGG ATATGTTTCC TCTTACCTGG GTTTTCTTAG     600
CTCTGTACTT TTCAGGACAC GAAGTGAGAA GCCAGCAAGA TCCACCCTGC GGAGGTCGGC     660
CGAATTCCAA AGATGCTGGC TACATCACTT CCCCAGGCTA CCCCCAGGAC TATCCCTCCC     720
ACCAGAACTG TGAGTGGATT GTCTACGCCC CCGAACCCAA CCAGAAGATT GTTCTCAACT     780
TCAACCCTCA CTTTGAAATC GAGAAACACG ACTGCAAGTA TGACTTCATT GAGATTCGGG     840
ATGGGGACAG TGAGTCAGCT GACCTCCTGG GCAAGCACTG TGGGAACATC GCCCCGCCCA     900
CCATCATCTC CTCAGGCTCC GTGTTATACA TCAAGTTCAC CTCAGACTAC GCCCGGCAGG     960
GGGCAGGTTT CTCTCTACGC TATGAGATCT TCAAAACAGG CTCTGAAGAT TGTTCCAAGA    1020
ACTTTACAAG CCCCAATGGG ACCATTGAAT CTCCAGGGTT TCCAGAGAAG TATCCACACA    1080
ATCTGGACTG TACCTTCACC ATCCTGGCCA AACCCAGGAT GGAGATCATC CTACAGTTCC    1140
TGACCTTTGA CCTGGAGCAT GACCCTCTAC AAGTGGGGGA AGGAGACTGT AAATATGACT    1200
GGCTGGACAT CTGGGATGGC ATTCCACATG TTGGACCTCT GATTGGCAAG TACTGTGGGA    1260
CGAAAACACC CTCCAAACTC CGCTCGTCCA CGGGGATCCT CTCCTTGACC TTTCACACGG    1320
ACATGGCAGT GGCCAAGGAT GGCTTCTCCG CACGTTACTA TTTGATCCAC CAGGAGCCAC    1380
CTGAGAATTT TCAGTGCAAT GTCCCTTTGG GAATGGAGTC TGGCCGGATT GCTAATGAAC    1440
AGATCAGTGC CTCCTCCACC TTCTCTGATG GGAGGTGGAC TCCTCAACAG AGCCGGCTCC    1500
ATGGTGATGA CAATGGCTGG ACACCCAATT TGGATTCCAA CAAGGAGTAT CTCCAGGTGG    1560
ACCTGCGCTT CCTAACCATG CTCACAGCCA TTGCAACACA GGGAGCCATT TCCAGGGAAA    1620
CCCAGAAAGG CTACTACGTC AAATCGTACA AGCTGGAAGT CAGCACAAAT GGTGAAGATT    1680
GGATGGTCTA CCGGCATGGC AAAAACCACA AGATATTCCA AGCGAACAAT GATGCGACCG    1740
AGGTGGTGCT AAACAAGCTC CACATGCCAC TGCTGACTCG GTTCATCAGG ATCCGCCCGC    1800
AGACGTGGCA TTTGGGCATT GCCCTTCGCC TGGAGCTCTT TGGCTGCCGG GTCACAGATG    1860
CACCCTGCTC CAACATGCTG GGGATGCTCT CGGGCCTCAT TGCTGATACC CAGATCTCTG    1920
CCTCCTCCAC CCGAGAGTAC CTCTGGAGCC CCAGTGCTGC CCGCCTGGTT AGTAGCCGCT    1980
CTGGCTGGTT TCCTCGGAAC CCTCAAGCCC AGCCAGGTGA AGAATGGCTT CAGGTAGACC    2040
TGGGGACACC CAAGACAGTG AAAGGGGTCA TCATCCAGGG AGCCCGAGGA GGAGACAGCA    2100
TCACTGCCGT GGAAGCCAGG GCGTTTGTAC GCAAGTTCAA AGTCTCCTAC AGCCTAAATG    2160
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GCAAGGACTG GGAATATATC CAGGACCCCA GGACTCAGCA GACAAAGCTG TTTGAAGGGA   2220
ACATGCACTA TGACACCCCT GACATCCGAA GGTTCGATCC TGTTCCAGCG CAGTATGTGC   2280
GGGTGTACCC AGAGAGGTGG TCGCCAGCAG GCATCGGGAT GAGGCTGGAG GTGCTGGGCT   2340
GTGACTGGAC AGACTCAAAG CCCACAGTGG AGACGCTGGG ACCCACCGTG AAGAGTGAAG   2400
AGACTACCAC CCCATATCCC ATGGATGAGG ATGCCACCGA GTGTGGGGAA AACTGCAGCT   2460
TTGAGGATGA CAAAGATTTG CAACTTCCTT CAGGATTCAA CTGCAACTTT GATTTTCCGG   2520
AAGAGACCTG TGGTTGGGTG TACGACCATG CCAAGTGGCT CCGGAGCACG TGGATCAGCA   2580
GCGCTAACCC CAATGACAGA ACATTTCCAG ATGACAAGAA CTTCTTGAAA CTGCAGAGTG   2640
ATGGCCGACG AGAGGGCCAG TACGGGCGGC TCATCAGCCC ACCGGTGCAC CTGCCCCGAA   2700
GCCCTGTGTG CATGGAGTTC CAGTACCAAG CCATGGGCGG CCACGGGGTG GCACTGCAGG   2760
TGGTTCGGGA AGCCAGCCAG GAAAGCAAAC TCCTTTGGGT CATCCGTGAG GACCAGGGCA   2820
GCGAGTGGAA GCACGGGCGC ATTATCCTGC CCAGCTATGA CATGGAGTAT CAGATCGTGT   2880
TCGAGGGAGT GATAGGGAAG GGACGATCGG GAGAGATTTC CATCGATGAC ATTCGGATAA   2940
GCACTGATGT CCCACTGGAG AACTGCATGG AACCCATATC AGCTTTTGCA GGGGGCACCC   3000
TCCCGCCAGG GACCGAGCCC ACAGTGGACA CGGTGCCCGT GCAGCCCATC CCAGCCTACT   3060
GGTATTACGT TATGGCGGCC GGGGGCGCCG TGCTGGTGCT GGCCTCCGTC GTCCTGGCCC   3120
TGGTGCTCCA CTACCACCGG TTCCGCTATG CGGCCAAGAA GACCGATCAC TCCATCACCT   3180
ACAAAACCTC CCACTACACC AACGGGGCCC CTCTGGCGGT CGAGCCCACC CTAACCATTA   3240
AGCTAGAGCA AGAGCGGGGC TCGCACTGCT GAGGGCCGAA GCAGGAACAG CGCCCCCCCA   3300
AAAAAAACCC AAGAAAGACT GCAAACACGT TGCCTCGATT TTGCACTTTT TTTCTCCTCG   3360
CCTAGTCTCT GTGTGAACCC TCAGACATCT CTCTCCAGGG TCCCCAACCC TGAGCGCTCT   3420
CATGTACCCC ACACCATTCT CTGTGGTTCT TGGTTCCGGT TTCTCTTTGC TCTGATATTG   3480
TTTGTTTTTA ATCATTATTT TTTTTCCTTT TCTTCTTTCC TTTTAATCTT CTCTCTTTTA   3540
TTCCTTTCTC CCCTCCCCGC CCCGCCTTTT TCTAATGATT TTAAACCAAC TCTAATGCTG   3600
CATCTGGAAT CCCAGAAGAG ACCCGCCCCT AAGCACTTCA CAACCCAAGG CTCTGTTGGT   3660
TTTGTTCCAG AGACAGGCCC TGTTGTTTTC TCCCCTTGCC TTATCCCATC CCTCCTCTCC   3720
TGGGCAGGCT GCCAGGTGTC TTGAGGGGAG CCTGGTCCTG TATGTATGTA CACAGTACAC   3780
TCCCATGTGA AGAGGTGTGT GTGTGTGTGT GTGTGTGTGT GTATTTTCGA GGGAGAGACT   3840
GATTCACTGT GGAAGGGGGG GAGTGTGGGT GTGTGTAGAG AGGGGCCCCT TCCCTCTTAT   3900
GTTGCTTCTT CTGGGGTACT TTTCAAGAAA ATAATATACT GTACACATTT TGTTTACTTG   3960
GAGAAGAGAT TGGAGCTTTT TTGTTGCCTT ATCTAGCTCT GGCTGGGTTT CTGTTGGCTG   4020
TCATTGTCAT CTCCAGGTAC CTAGACAAAT AGAGACCATT GGGAATGCAA TGTGGCTTCA   4080
CCCATCCTTA TCCCCATCCC AAGCCACCCA AGACTATGGT TCCTCCAGTG CACTCAGACA   4140
TGACCCCTTT TGTTATGTTT CCTGGTGTCT TTGAAGTCAC AAGATAACAG CCATTGGGTG   4200
CATGGAGTCA TTTCTACTTC CAGCCCTGAA GCAAATGTGT CTCATGTTGC CTTATAAAAA   4260
AAACCGGAAT TCCTGTAGTT GAAGAGTAAG ATTTTGTACG GTACATTTTT AATGACAGCT   4320
TGGATATTGG AATACTCAAC TTTTGTTGTA GCCAATGAGA GGGATATGCC ACTAATGGTA   4380
TCTAAATCAT ACAGTACGTA CTTTAGGATG GGGACAAAAA TCACAACGAT TTATTTATTT   4440
ATTTACTTAG TGTATGTGAG TGCACTGTTG GTGTCTTCAG ACACACCAGA AGATGACTTC   4500
AGATCCGATT ACATATGGGT TGTGAGCCAC CATGTGGTTG CTGGGATTTG AACTCTGGAC   4560
CTCTGGAAGA GCAGTCAGTG CTTGTAACTC TGAGCCATCT TTCTAGCCCC CCCCCCCCCC   4620
CCGCTATCTT TTAGAAATGT AATTTGCCAT ACTTTGAGCA ATGTTCTTGA TGTCATTAGG   4680
ATATTTCACA GATAACTTCA CTTAAGATAA TTAGAGCAAA AAAAAAAAAA AAAAAAAAAA   4740
AAAAAAAAAA AAAAAAAAAA AAAAA                                         4765
```

(2) INFORMATION FOR SEQ ID NO:22:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 901 amino acids

(B) TYPE: amino acid

(C) STRANDEDNESS: single

(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:22:

```
Met Asp Met Phe Pro Leu Thr Trp Val Phe Leu Ala Leu Tyr Phe Ser
1               5                  10                  15
Gly His Glu Val Arg Ser Gln Gln Asp Pro Pro Cys Gly Gly Arg Pro
            20                  25                  30
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Asn Ser Lys Asp Ala Gly Tyr Ile Thr Ser Pro Gly Tyr Pro Gln Asp
        35                  40                  45
Tyr Pro Ser His Gln Asn Cys Glu Trp Ile Val Tyr Ala Pro Glu Pro
    50                  55                  60
Asn Gln Lys Ile Val Leu Asn Phe Asn Pro His Phe Glu Ile Glu Lys
65                  70                  75                  80
His Asp Cys Lys Tyr Asp Phe Ile Glu Ile Arg Asp Gly Asp Ser Glu
                85                  90                  95
Ser Ala Asp Leu Leu Gly Lys His Cys Gly Asn Ile Ala Pro Pro Thr
            100                 105                 110
Ile Ile Ser Ser Gly Ser Val Leu Tyr Ile Lys Phe Thr Ser Asp Tyr
        115                 120                 125
Ala Arg Gln Gly Ala Gly Phe Ser Leu Arg Tyr Glu Ile Phe Lys Thr
    130                 135                 140
Gly Ser Glu Asp Cys Ser Lys Asn Phe Thr Ser Pro Asn Gly Thr Ile
145                 150                 155                 160
Glu Ser Pro Gly Phe Pro Glu Lys Tyr Pro His Asn Leu Asp Cys Thr
                165                 170                 175
Phe Thr Ile Leu Ala Lys Pro Arg Met Glu Ile Ile Leu Gln Phe Leu
            180                 185                 190
Thr Phe Asp Leu Glu His Asp Pro Leu Gln Val Gly Glu Gly Asp Cys
        195                 200                 205
Lys Tyr Asp Trp Leu Asp Ile Trp Asp Gly Ile Pro His Val Gly Pro
    210                 215                 220
Leu Ile Gly Lys Tyr Cys Gly Thr Lys Thr Pro Ser Lys Leu Arg Ser
225                 230                 235                 240
Ser Thr Gly Ile Leu Ser Leu Thr Phe His Thr Asp Met Ala Val Ala
                245                 250                 255
Lys Asp Gly Phe Ser Ala Arg Tyr Tyr Leu Ile His Gln Glu Pro Pro
            260                 265                 270
Glu Asn Phe Gln Cys Asn Val Pro Leu Gly Met Glu Ser Gly Arg Ile
        275                 280                 285
Ala Asn Glu Gln Ile Ser Ala Ser Ser Thr Phe Ser Asp Gly Arg Trp
    290                 295                 300
Thr Pro Gln Gln Ser Arg Leu His Gly Asp Asp Asn Gly Trp Thr Pro
305                 310                 315                 320
Asn Leu Asp Ser Asn Lys Glu Tyr Leu Gln Val Asp Leu Arg Phe Leu
                325                 330                 335
Thr Met Leu Thr Ala Ile Ala Thr Gln Gly Ala Ile Ser Arg Glu Thr
            340                 345                 350
Gln Lys Gly Tyr Tyr Val Lys Ser Tyr Lys Leu Glu Val Ser Thr Asn
        355                 360                 365
Gly Glu Asp Trp Met Val Tyr Arg His Gly Lys Asn His Lys Ile Phe
    370                 375                 380
Gln Ala Asn Asn Asp Ala Thr Glu Val Val Leu Asn Lys Leu His Met
385                 390                 395                 400
Pro Leu Leu Thr Arg Phe Ile Arg Ile Arg Pro Gln Thr Trp His Leu
                405                 410                 415
Gly Ile Ala Leu Arg Leu Glu Leu Phe Gly Cys Arg Val Thr Asp Ala
            420                 425                 430
Pro Cys Ser Asn Met Leu Gly Met Leu Ser Gly Leu Ile Ala Asp Thr
        435                 440                 445
Gln Ile Ser Ala Ser Ser Thr Arg Glu Tyr Leu Trp Ser Pro Ser Ala
    450                 455                 460
Ala Arg Leu Val Ser Ser Arg Ser Gly Trp Phe Pro Arg Asn Pro Gln
465                 470                 475                 480
Ala Gln Pro Gly Glu Glu Trp Leu Gln Val Asp Leu Gly Thr Pro Lys
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                485                 490                 495
Thr Val Lys Gly Val Ile Ile Gln Gly Ala Arg Gly Gly Asp Ser Ile
            500                 505                 510
Thr Ala Val Glu Ala Arg Ala Phe Val Arg Lys Phe Lys Val Ser Tyr
        515                 520                 525
Ser Leu Asn Gly Lys Asp Trp Glu Tyr Ile Gln Asp Pro Arg Thr Gln
    530                 535                 540
Gln Thr Lys Leu Phe Glu Gly Asn Met His Tyr Asp Thr Pro Asp Ile
545                 550                 555                 560
Arg Arg Phe Asp Pro Val Pro Ala Gln Tyr Val Arg Val Tyr Pro Glu
                565                 570                 575
Arg Trp Ser Pro Ala Gly Ile Gly Met Arg Leu Glu Val Leu Gly Cys
            580                 585                 590
Asp Trp Thr Asp Ser Lys Pro Thr Val Glu Thr Leu Gly Pro Thr Val
        595                 600                 605
Lys Ser Glu Glu Thr Thr Thr Pro Tyr Pro Met Asp Glu Asp Ala Thr
    610                 615                 620
Glu Cys Gly Glu Asn Cys Ser Phe Glu Asp Asp Lys Asp Leu Gln Leu
625                 630                 635                 640
Pro Ser Gly Phe Asn Cys Asn Phe Asp Phe Pro Glu Glu Thr Cys Gly
                645                 650                 655
Trp Val Tyr Asp His Ala Lys Trp Leu Arg Ser Thr Trp Ile Ser Ser
            660                 665                 670
Ala Asn Pro Asn Asp Arg Thr Phe Pro Asp Asp Lys Asn Phe Leu Lys
        675                 680                 685
Leu Gln Ser Asp Gly Arg Arg Glu Gly Gln Tyr Gly Arg Leu Ile Ser
    690                 695                 700
Pro Pro Val His Leu Pro Arg Ser Pro Val Cys Met Glu Phe Gln Tyr
705                 710                 715                 720
Gln Ala Met Gly Gly His Gly Val Ala Leu Gln Val Val Arg Glu Ala
                725                 730                 735
Ser Gln Glu Ser Lys Leu Leu Trp Val Ile Arg Glu Asp Gln Gly Ser
            740                 745                 750
Glu Trp Lys His Gly Arg Ile Ile Leu Pro Ser Tyr Asp Met Glu Tyr
        755                 760                 765
Gln Ile Val Phe Glu Gly Val Ile Gly Lys Gly Arg Ser Gly Glu Ile
    770                 775                 780
Ser Ile Asp Asp Ile Arg Ile Ser Thr Asp Val Pro Leu Glu Asn Cys
785                 790                 795                 800
Met Glu Pro Ile Ser Ala Phe Ala Gly Gly Thr Leu Pro Pro Gly Thr
                805                 810                 815
Glu Pro Thr Val Asp Thr Val Pro Val Gln Pro Ile Pro Ala Tyr Trp
            820                 825                 830
Tyr Tyr Val Met Ala Ala Gly Gly Ala Val Leu Val Leu Ala Ser Val
        835                 840                 845
Val Leu Ala Leu Val Leu His Tyr His Arg Phe Arg Tyr Ala Ala Lys
    850                 855                 860
Lys Thr Asp His Ser Ile Thr Tyr Lys Thr Ser His Tyr Thr Asn Gly
865                 870                 875                 880
Ala Pro Leu Ala Val Glu Pro Thr Leu Thr Ile Lys Leu Glu Gln Glu
                885                 890                 895
Arg Gly Ser His Cys
            900
```

(2) INFORMATION FOR SEQ ID NO:23:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 4780 base pairs

none SE2(b)5

(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: cDNA

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:23:

AAACTGGAGC TCCACCGCGG TGGCGGCCGC CCGGGCAGGT CTAGAATTCA GCGGCCGCTG 60
AATTCTATCC AGCGGTCGGT GCCTCTGCCC GCGTGTGTGT CCCGGGTGCC GGGGGACCTG 120
TGTCAGTTAG CGCTTCTGAG ATCACACAGC TGCCTAGGGG CCGTGTGATG CCCAGGGCAA 180
TTCTTGGCTT TGATTTTTAT TATTATTACT ATTATTTTGC GTTCAGCTTT CGGGAAACCC 240
TCGTGATGTT GTAGGATAAA GGAAATGACA CTTTGAGGAA CTGGAGAGAA CATACACGCG 300
TTTGGGTTTG AAGAGGAAAC CGGTCTCCGC TTCCTTAGCT TGCTCCCTCT TTGCTGATTT 360
CAAGAGCTAT CTCCTATGAG GTGGAGATAT TCCAGCAAGA ATAAAGGTGA AGACAGACTG 420
ACTGCCAGGA CCCAGGAGGA AAACGTTGAT CGTTAGAGAC CTTTGCAGAA GACACCACCA 480
GGAGGAAAAT TAGAGAGGAA AAACACAAAG ACATAATTAT AGGAGATCCC ACAAACCTAG 540
CCCGGGAGAG AGCCTCTCTG TCAAAAATGG ATATGTTTCC TCTTACCTGG GTTTTCTTAG 600
CTCTGTACTT TTCAGGACAC GAAGTGAGAA GCCAGCAAGA TCCACCCTGC GGAGGTCGGC 660
CGAATTCCAA AGATGCTGGC TACATCACTT CCCCAGGCTA CCCCCAGGAC TATCCCTCCC 720
ACCAGAACTG TGAGTGGATT GTCTACGCCC CCGAACCCAA CCAGAAGATT GTTCTCAACT 780
TCAACCCTCA CTTTGAAATC GAGAAACACG ACTGCAAGTA TGACTTCATT GAGATTCGGG 840
ATGGGGACAG TGAGTCAGCT GACCTCCTGG GCAAGCACTG TGGGAACATC GCCCCGCCCA 900
CCATCATCTC CTCAGGCTCC GTGTTATACA TCAAGTTCAC CTCAGACTAC GCCCGGCAGG 960
GGGCAGGTTT CTCTCTACGC TATGAGATCT TCAAAACAGG CTCTGAAGAT TGTTCCAAGA 1020
ACTTTACAAG CCCCAATGGG ACCATTGAAT CTCCAGGGTT TCCAGAGAAG TATCCACACA 1080
ATCTGGACTG TACCTTCACC ATCCTGGCCA AACCCAGGAT GGAGATCATC CTACAGTTCC 1140
TGACCTTTGA CCTGGAGCAT GACCCTCTAC AAGTGGGGGA AGGAGACTGT AAATATGACT 1200
GGCTGGACAT CTGGGATGGC ATTCCACATG TTGGACCTCT GATTGGCAAG TACTGTGGGA 1260
CGAAAACACC CTCCAAACTC CGCTCGTCCA CGGGGATCCT CTCCTTGACC TTTCACACGG 1320
ACATGGCAGT GGCCAAGGAT GGCTTCTCCG CACGTTACTA TTTGATCCAC CAGGAGCCAC 1380
CTGAGAATTT TCAGTGCAAT GTCCCTTTGG GAATGGAGTC TGGCCGGATT GCTAATGAAC 1440
AGATCAGTGC CTCCTCCACC TTCTCTGATG GGAGGTGGAC TCCTCAACAG AGCCGGCTCC 1500
ATGGTGATGA CAATGGCTGG ACACCCAATT TGGATTCCAA CAAGGAGTAT CTCCAGGTGG 1560
ACCTGCGCTT CCTAACCATG CTCACAGCCA TTGCAACACA GGGAGCCATT TCCAGGGAAA 1620
CCCAGAAAGG CTACTACGTC AAATCGTACA AGCTGGAAGT CAGCACAAAT GGTGAAGATT 1680
GGATGGTCTA CCGGCATGGC AAAAACCACA AGATATTCCA AGCGAACAAT GATGCGACCG 1740
AGGTGGTGCT AAACAAGCTC CACATGCCAC TGCTGACTCG GTTCATCAGG ATCCGCCCGC 1800
AGACGTGGCA TTTGGGCATT GCCCTTCGCC TGGAGCTCTT TGGCTGCCGG GTCACAGATG 1860
CACCCTGCTC CAACATGCTG GGGATGCTCT CGGGCCTCAT TGCTGATACC CAGATCTCTG 1920
CCTCCTCCAC CCGAGAGTAC CTCTGGAGCC CCAGTGCTGC CCGCCTGGTT AGTAGCCGCT 1980
CTGGCTGGTT TCCTCGGAAC CCTCAAGCCC AGCCAGGTGA AGAATGGCTT CAGGTAGACC 2040
TGGGGACACC CAAGACAGTG AAAGGGGTCA TCATCCAGGG AGCCCGAGGA GGAGACAGCA 2100
TCACTGCCGT GGAAGCCAGG GCGTTTGTAC GCAAGTTCAA AGTCTCCTAC AGCCTAAATG 2160
GCAAGGACTG GGAATATATC CAGGACCCCA GGACTCAGCA GACAAAGCTG TTTGAAGGGA 2220
ACATGCACTA TGACACCCCT GACATCCGAA GGTTCGATCC TGTTCCAGCG CAGTATGTGC 2280
GGGTGTACCC AGAGAGGTGG TCGCCAGCAG GCATCGGGAT GAGGCTGGAG GTGCTGGGCT 2340
GTGACTGGAC AGACTCAAAG CCCACAGTGG AGACGCTGGG ACCCACCGTG AAGAGTGAAG 2400
AGACTACCAC CCCATATCCC ATGGATGAGG ATGCCACCGA GTGTGGGGAA AACTGCAGCT 2460
TTGAGGATGA CAAAGATTTG CAACTTCCTT CAGGATTCAA CTGCAACTTT GATTTTCCGG 2520
AAGAGACCTG TGGTTGGGTG TACGACCATG CCAAGTGGCT CCGGAGCACG TGGATCAGCA 2580
GCGCTAACCC CAATGACAGA ACATTTCCAG ATGACAAGAA CTTCTTGAAA CTGCAGAGTG 2640
ATGGCCGACG AGAGGGCCAG TACGGGCGGC TCATCAGCCC ACCGGTGCAC CTGCCCCGAA 2700
GCCCTGTGTG CATGGAGTTC CAGTACCAAG CCATGGGCGG CCACGGGGTG GCACTGCAGG 2760
TGGTTCGGGA AGCCAGCCAG GAAAGCAAAC TCCTTTGGGT CATCCGTGAG GACCAGGGCA 2820
GCGAGTGGAA GCACGGGCGC ATTATCCTGC CCAGCTATGA CATGGAGTAT CAGATCGTGT 2880
TCGAGGGAGT GATAGGGAAG GGACGATCGG GAGAGATTTC CATCGATGAC ATTCGGATAA 2940
GCACTGATGT CCCACTGGAG AACTGCATGG AACCCATATC AGCTTTTGCA GGTGAGGATT 3000
TTAAAGGGGG CACCCTCCCG CCAGGGACCG AGCCCACAGT GGACACGGTG CCCGTGCAGC 3060
CCATCCCAGC CTACTGGTAT TACGTTATGG CGGCCGGGGG CGCCGTGCTG GTGCTGGCCT 3120

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CCGTCGTCCT GGCCCTGGTG CTCCACTACC ACCGGTTCCG CTATGCGGCC AAGAAGACCG    3180
ATCACTCCAT CACCTACAAA ACCTCCCACT ACACCAACGG GGCCCCTCTG GCGGTCGAGC    3240
CCACCCTAAC CATTAAGCTA GAGCAAGAGC GGGGCTCGCA CTGCTGAGGG CCGAAGCAGG    3300
AACAGCGCCC CCCCAAAAAA AACCCAAGAA AGACTGCAAA CACGTTGCCT CGATTTTGCA    3360
CTTTTTTTCT CCTCGCCTAG TCTCTGTGTG AACCCTCAGA CATCTCTCTC CAGGGTCCCC    3420
AACCCTGAGC GCTCTCATGT ACCCCACACC ATTCTCTGTG GTTCTTGGTT CCGGTTTCTC    3480
TTTGCTCTGA TATTGTTTGT TTTTAATCAT TATTTTTTTT CCTTTTCTTC TTTCCTTTTA    3540
ATCTTCTCTC TTTTATTCCT TTCTCCCCTC CCCGCCCCGC CTTTTTCTAA TGATTTTAAA    3600
CCAACTCTAA TGCTGCATCT GGAATCCCAG AAGAGACCCG CCCCTAAGCA CTTCACAACC    3660
CAAGGCTCTG TTGGTTTTGT TCCAGAGACA GGCCCTGTTG TTTTCTCCCC TTGCCTTATC    3720
CCATCCCTCC TCTCCTGGGC AGGCTGCCAG GTGTCTTGAG GGGAGCCTGG TCCTGTATGT    3780
ATGTACACAG TACACTCCCA TGTGAAGAGG TGTGTGTGTG TGTGTGTGTG TGTGTGTATT    3840
TTCGAGGGAG AGACTGATTC ACTGTGGAAG GGGGGGAGTG TGGGTGTGTG TAGAGAGGGG    3900
CCCCTTCCCT CTTATGTTGC TTCTTCTGGG GTACTTTTCA AGAAAATAAT ATACTGTACA    3960
CATTTTGTTT ACTTGGAGAA GAGATTGGAG CTTTTTTGTT GCCTTATCTA GCTCTGGCTG    4020
GGTTTCTGTT GGCTGTCATT GTCATCTCCA GGTACCTAGA CAAATAGAGA CCATTGGGAA    4080
TGCAATGTGG CTTCACCCAT CCTTATCCCC ATCCCAAGCC ACCCAAGACT ATGGTTCCTC    4140
CAGTGCACTC AGACATGACC CCTTTTGTTA TGTTTCCTGG TGTCTTTGAA GTCACAAGAT    4200
AACAGCCATT GGGTGCATGG AGTCATTTCT ACTTCCAGCC CTGAAGCAAA TGTGTCTCAT    4260
GTTGCCTTAT AAAAAAAACC GGAATTCCTG TAGTTGAAGA GTAAGATTTT GTACGGTACA    4320
TTTTTAATGA CAGCTTGGAT ATTGGAATAC TCAACTTTTG TTGTAGCCAA TGAGAGGGAT    4380
ATGCCACTAA TGGTATCTAA ATCATACAGT ACGTACTTTA GGATGGGGAC AAAAATCACA    4440
ACGATTTATT TATTTATTTA CTTAGTGTAT GTGAGTGCAC TGTTGGTGTC TTCAGACACA    4500
CCAGAAGATG ACTTCAGATC CGATTACATA TGGGTTGTGA GCCACCATGT GGTTGCTGGG    4560
ATTTGAACTC TGGACCTCTG GAAGAGCAGT CAGTGCTTGT AACTCTGAGC CATCTTTCTA    4620
GCCCCCCCCC CCCCCCCGCT ATCTTTTAGA AATGTAATTT GCCATACTTT GAGCAATGTT    4680
CTTGATGTCA TTAGGATATT TCACAGATAA CTTCACTTAA GATAATTAGA GCAAAAAAAA    4740
AAAAAAAAAA AAAAAAAAAA AAAAAAAAAA AAAAAAAAAA                          4780
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(2) INFORMATION FOR SEQ ID NO:24:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 906 amino acids

(B) TYPE: amino acid

(C) STRANDEDNESS: single

(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:24:

```
Met Asp Met Phe Pro Leu Thr Trp Val Phe Leu Ala Leu Tyr Phe Ser
1               5                  10                  15
Gly His Glu Val Arg Ser Gln Gln Asp Pro Pro Cys Gly Gly Arg Pro
            20                  25                  30
Asn Ser Lys Asp Ala Gly Tyr Ile Thr Ser Pro Gly Tyr Pro Gln Asp
        35                  40                  45
Tyr Pro Ser His Gln Asn Cys Glu Trp Ile Val Tyr Ala Pro Glu Pro
    50                  55                  60
Asn Gln Lys Ile Val Leu Asn Phe Asn Pro His Phe Glu Ile Glu Lys
65                  70                  75                  80
His Asp Cys Lys Tyr Asp Phe Ile Glu Ile Arg Asp Gly Asp Ser Glu
                85                  90                  95
Ser Ala Asp Leu Leu Gly Lys His Cys Gly Asn Ile Ala Pro Pro Thr
            100                 105                 110
Ile Ile Ser Ser Gly Ser Val Leu Tyr Ile Lys Phe Thr Ser Asp Tyr
        115                 120                 125
Ala Arg Gln Gly Ala Gly Phe Ser Leu Arg Tyr Glu Ile Phe Lys Thr
    130                 135                 140
Gly Ser Glu Asp Cys Ser Lys Asn Phe Thr Ser Pro Asn Gly Thr Ile
145                 150                 155                 160
```

```
Glu Ser Pro Gly Phe Pro Glu Lys Tyr Pro His Asn Leu Asp Cys Thr
                  165                 170                 175
Phe Thr Ile Leu Ala Lys Pro Arg Met Glu Ile Ile Leu Gln Phe Leu
             180                 185                 190
Thr Phe Asp Leu Glu His Asp Pro Leu Gln Val Gly Glu Gly Asp Cys
         195                 200                 205
Lys Tyr Asp Trp Leu Asp Ile Trp Asp Gly Ile Pro His Val Gly Pro
     210                 215                 220
Leu Ile Gly Lys Tyr Cys Gly Thr Lys Thr Pro Ser Lys Leu Arg Ser
225                 230                 235                 240
Ser Thr Gly Ile Leu Ser Leu Thr Phe His Thr Asp Met Ala Val Ala
                245                 250                 255
Lys Asp Gly Phe Ser Ala Arg Tyr Tyr Leu Ile His Gln Glu Pro Pro
            260                 265                 270
Glu Asn Phe Gln Cys Asn Val Pro Leu Gly Met Glu Ser Gly Arg Ile
        275                 280                 285
Ala Asn Glu Gln Ile Ser Ala Ser Ser Thr Phe Ser Asp Gly Arg Trp
    290                 295                 300
Thr Pro Gln Gln Ser Arg Leu His Gly Asp Asp Asn Gly Trp Thr Pro
305                 310                 315                 320
Asn Leu Asp Ser Asn Lys Glu Tyr Leu Gln Val Asp Leu Arg Phe Leu
                325                 330                 335
Thr Met Leu Thr Ala Ile Ala Thr Gln Gly Ala Ile Ser Arg Glu Thr
            340                 345                 350
Gln Lys Gly Tyr Tyr Val Lys Ser Tyr Lys Leu Glu Val Ser Thr Asn
        355                 360                 365
Gly Glu Asp Trp Met Val Tyr Arg His Gly Lys Asn His Lys Ile Phe
    370                 375                 380
Gln Ala Asn Asn Asp Ala Thr Glu Val Val Leu Asn Lys Leu His Met
385                 390                 395                 400
Pro Leu Leu Thr Arg Phe Ile Arg Ile Arg Pro Gln Thr Trp His Leu
                405                 410                 415
Gly Ile Ala Leu Arg Leu Glu Leu Phe Gly Cys Arg Val Thr Asp Ala
            420                 425                 430
Pro Cys Ser Asn Met Leu Gly Met Leu Ser Gly Leu Ile Ala Asp Thr
        435                 440                 445
Gln Ile Ser Ala Ser Ser Thr Arg Glu Tyr Leu Trp Ser Pro Ser Ala
    450                 455                 460
Ala Arg Leu Val Ser Ser Arg Ser Gly Trp Phe Pro Arg Asn Pro Gln
465                 470                 475                 480
Ala Gln Pro Gly Glu Glu Trp Leu Gln Val Asp Leu Gly Thr Pro Lys
                485                 490                 495
Thr Val Lys Gly Val Ile Ile Gln Gly Ala Arg Gly Gly Asp Ser Ile
            500                 505                 510
Thr Ala Val Glu Ala Arg Ala Phe Val Arg Lys Phe Lys Val Ser Tyr
        515                 520                 525
Ser Leu Asn Gly Lys Asp Trp Glu Tyr Ile Gln Asp Pro Arg Thr Gln
    530                 535                 540
Gln Thr Lys Leu Phe Glu Gly Asn Met His Tyr Asp Thr Pro Asp Ile
545                 550                 555                 560
Arg Arg Phe Asp Pro Val Pro Ala Gln Tyr Val Arg Val Tyr Pro Glu
                565                 570                 575
Arg Trp Ser Pro Ala Gly Ile Gly Met Arg Leu Glu Val Leu Gly Cys
            580                 585                 590
Asp Trp Thr Asp Ser Lys Pro Thr Val Glu Thr Leu Gly Pro Thr Val
        595                 600                 605
Lys Ser Glu Glu Thr Thr Thr Pro Tyr Pro Met Asp Glu Asp Ala Thr
```

```
     610                 615                 620
Glu Cys Gly Glu Asn Cys Ser Phe Glu Asp Asp Lys Asp Leu Gln Leu
625                 630                 635                 640
Pro Ser Gly Phe Asn Cys Asn Phe Asp Phe Pro Glu Glu Thr Cys Gly
                645                 650                 655
Trp Val Tyr Asp His Ala Lys Trp Leu Arg Ser Thr Trp Ile Ser Ser
            660                 665                 670
Ala Asn Pro Asn Asp Arg Thr Phe Pro Asp Asp Lys Asn Phe Leu Lys
        675                 680                 685
Leu Gln Ser Asp Gly Arg Arg Glu Gly Gln Tyr Gly Arg Leu Ile Ser
    690                 695                 700
Pro Pro Val His Leu Pro Arg Ser Pro Val Cys Met Glu Phe Gln Tyr
705                 710                 715                 720
Gln Ala Met Gly Gly His Gly Val Ala Leu Gln Val Val Arg Glu Ala
                725                 730                 735
Ser Gln Glu Ser Lys Leu Leu Trp Val Ile Arg Glu Asp Gln Gly Ser
            740                 745                 750
Glu Trp Lys His Gly Arg Ile Ile Leu Pro Ser Tyr Asp Met Glu Tyr
        755                 760                 765
Gln Ile Val Phe Glu Gly Val Ile Gly Lys Gly Arg Ser Gly Glu Ile
    770                 775                 780
Ser Ile Asp Asp Ile Arg Ile Ser Thr Asp Val Pro Leu Glu Asn Cys
785                 790                 795                 800
Met Glu Pro Ile Ser Ala Phe Ala Gly Glu Asp Phe Lys Gly Gly Thr
                805                 810                 815
Leu Pro Pro Gly Thr Glu Pro Thr Val Asp Thr Val Pro Val Gln Pro
            820                 825                 830
Ile Pro Ala Tyr Trp Tyr Tyr Val Met Ala Ala Gly Gly Ala Val Leu
        835                 840                 845
Val Leu Ala Ser Val Val Leu Ala Leu Val Leu His Tyr His Arg Phe
    850                 855                 860
Arg Tyr Ala Ala Lys Lys Thr Asp His Ser Ile Thr Tyr Lys Thr Ser
865                 870                 875                 880
His Tyr Thr Asn Gly Ala Pro Leu Ala Val Glu Pro Thr Leu Thr Ile
                885                 890                 895
Lys Leu Glu Gln Glu Arg Gly Ser His Cys
            900                 905
```

(2) INFORMATION FOR SEQ ID NO:25:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 195 base pairs

(B) TYPE: nucleic acid

(C) STRANDEDNESS: single

(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: cDNA

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:25:

```
TTCGAGGGAG TGATAGGGAA AGGACGTTCC GGAGAGATTG CCATTGATGA CATTCGGATA      60
AGCACTGATG TCCCACTGGA GAACTGCATG GAACCCATCT CGGCTTTTGC AGGGGGCACC     120
CTCCTGCCAG GGACCGAGCC CACAGTGGAC ACGGTGCCCA TGCAGCCCAT CCCAGCCTAC     180
TGGTATTACG TAATG                                                     195
```

(2) INFORMATION FOR SEQ ID NO:26:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 65 amino acids

(B) TYPE: amino acid

(C) STRANDEDNESS: single

(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:26:

```
Phe Glu Gly Val Ile Gly Lys Gly Arg Ser Gly Glu Ile Ala Ile Asp
1               5                  10                  15
Asp Ile Arg Ile Ser Thr Asp Val Pro Leu Glu Asn Cys Met Glu Pro
            20                  25                  30
Ile Ser Ala Phe Ala Gly Gly Thr Leu Leu Pro Gly Thr Glu Pro Thr
        35                  40                  45
Val Asp Thr Val Pro Met Gln Pro Ile Pro Ala Tyr Trp Tyr Tyr Val
    50                  55                  60
Met
65
```

WHAT IS CLAIMED IS:

1. An isolated polypeptide comprising the amino acid sequence of SEQ ID NO:2, 4, 8, 10, 12, 14, 16, 18, 20, 22 or 24, or a deletion mutant thereof comprising at least an 8 residue domain thereof found in neither mouse, chick nor drosphila neuropilin-1 cDNA nor SEQ ID NO:26, wherein said polypeptide has an activity selected from at least one of: a semaphorin binding or binding inhibitory activity, a neuron modulating or modulting inhibitory activity and a semaphorin receptor specific antigenicity or immunogenicity.

2. The isolated polypeptide of claim 1, comprising the amino acid sequence of SEQ ID NO:2, 18 or 20 or a deletion mutant thereof, wherein said domain comprises a human specific SR sequence.

3. An isolated or recombinant first nucleic acid comprising a strand of SEQ ID NO:1, 3, 7, 9, 11, 13, 15, 17, 19, 21 or 23 or at least 24 consecutive bases of SEQ ID NO:1, 3, 7, 9, 11, 13, 15, 17, 19, 21 or 23 and sufficient to specifically hybridize with a second nucleic acid comprising SEQ ID NO:1, 3, 7, 9, 11, 13, 15, 17, 19, 21 or 23, respectively, in the presence of mouse, chick and drosophilia neuropilin-1 cDNA.

4. A recombinant nucleic acid encoding a polypeptide according to claim 1.

5. A cell comprising a nucleic acid according to claim 4.

6. An antibody which specifically binds a polypeptide according to claim 1.

7. A method of making an SR polypeptide said method comprising steps: introducing a nucleic acid according to claim 4 into a host cell or cellular extract, incubating said host cell or extract under conditions whereby said nucleic acid is expressed as a transcript and said transcript is expressed as a translation product comprising said polypeptide, and isolating said translation product.

8. A method of modulating a cell comprising at least one of a SR polypeptide and a semaphorin, said method comprising the step of modulating the interaction of the SR

polypeptide and the semaphorin by contacting the cell with an effective amount of a composition comprising an inhibitor of the interaction, where by a characteristic of the cell is modulated, wherein said cell is a neuron, said characteristic is axon outgrowth and/or guidance and said inhibitor is a polypeptide according to claim 1.

9. A method of screening for an agent which modulates the interaction of a SR polypeptide to a binding target, said method comprising the steps of:

incubating a mixture comprising:

an isolated polypeptide according to claim 1,

a binding target of said polypeptide, and

a candidate agent;

under conditions whereby, but for the presence of said agent, said polypeptide specifically binds said binding target at a reference affinity;

detecting the binding affinity of said polypeptide to said binding target to determine an agent-biased affinity,

wherein a difference between the agent-biased affinity and the reference affinity indicates that said agent modulates the binding of said polypeptide to said binding target.

10. A method according to claim 9, wherein said binding target is a semaphorin polypeptide.

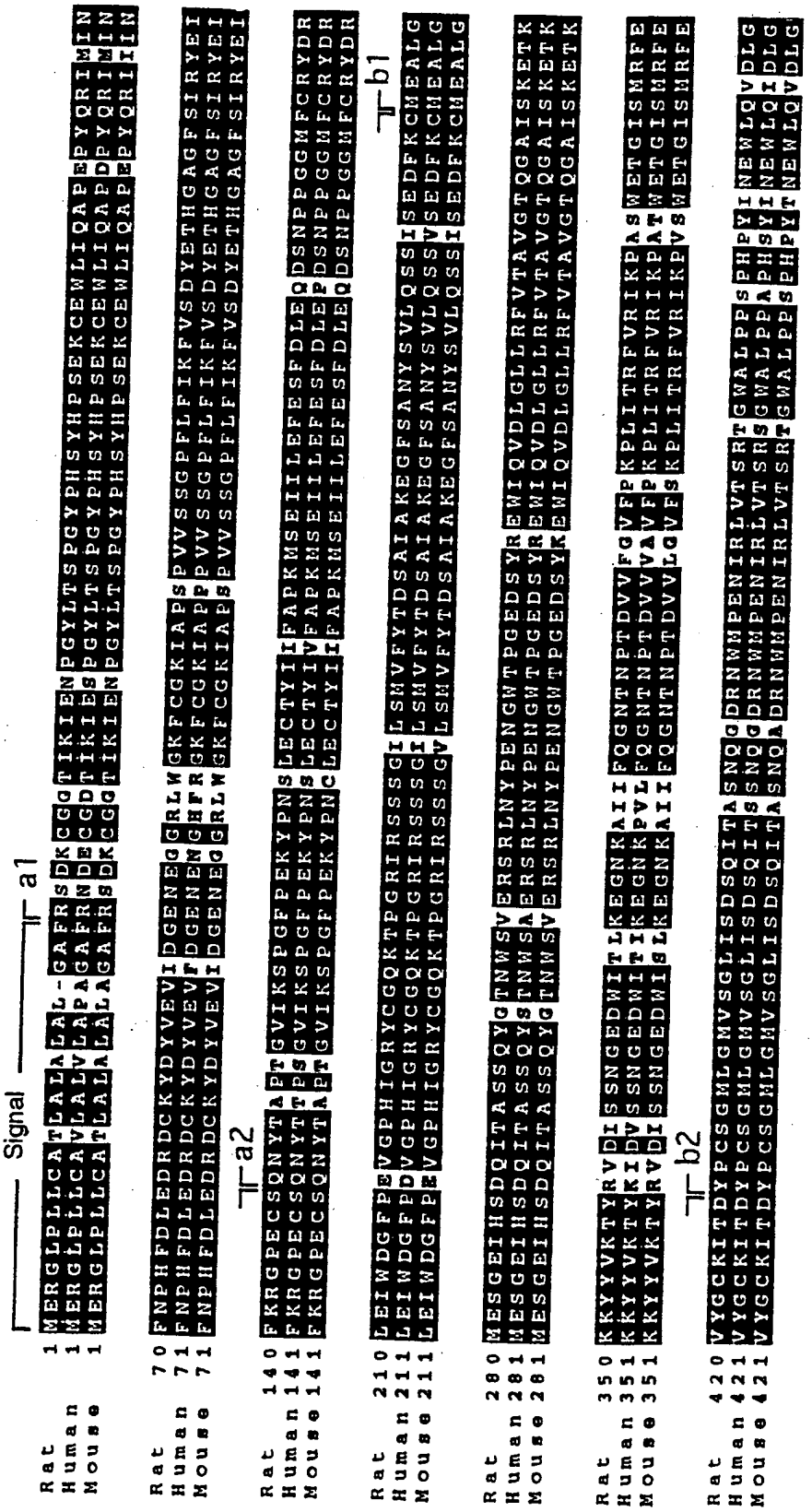

FIG. 1A1

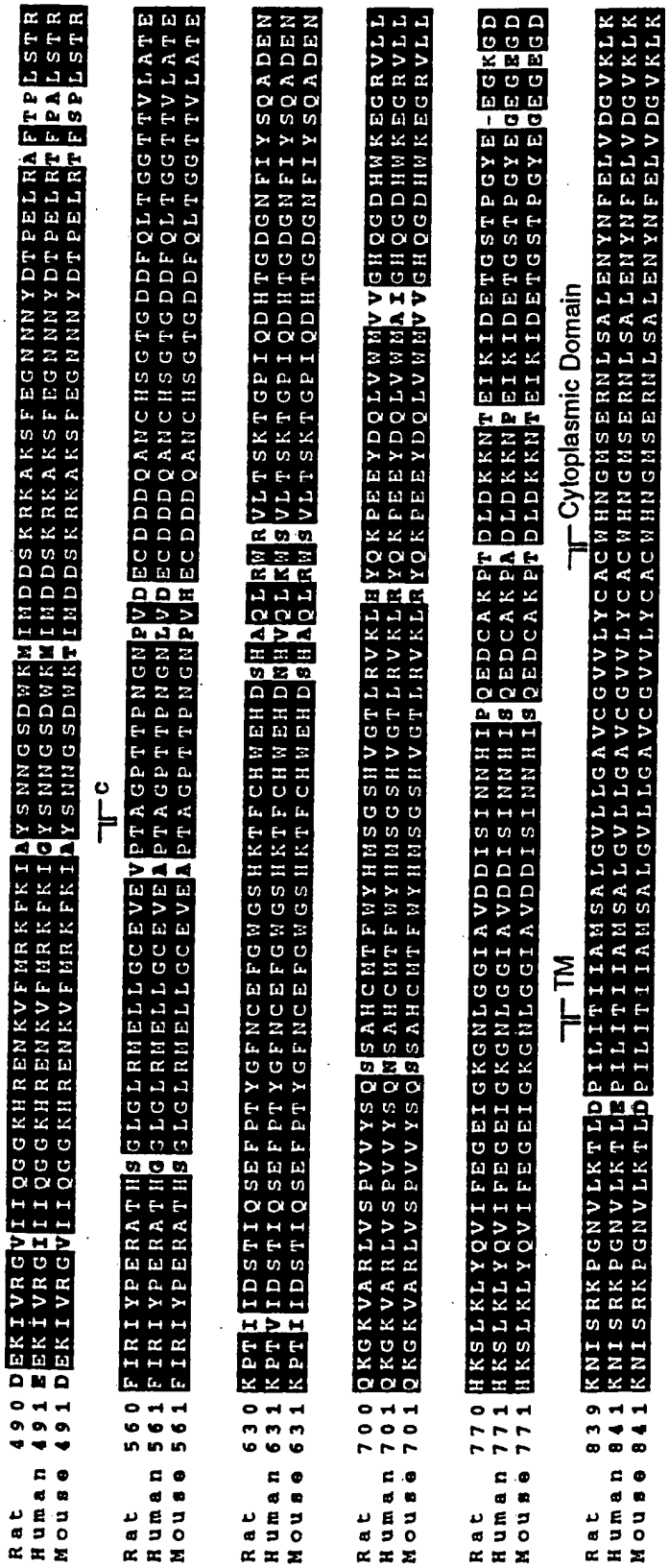

FIG. 1A2

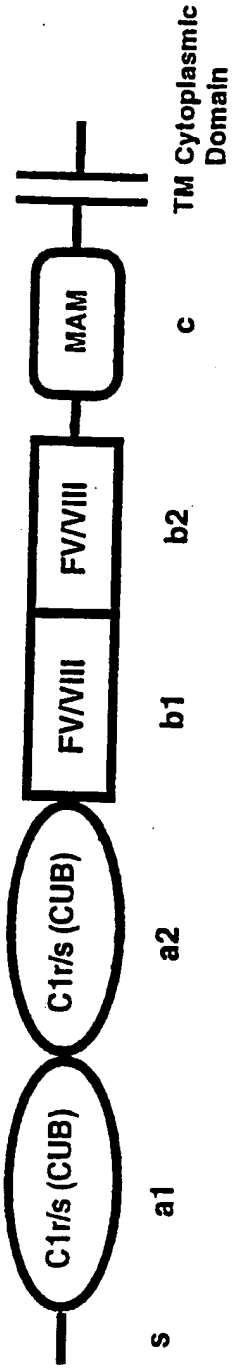
C1r/s (CUB)
C1r/s (CUB)
FV/VIII
FV/VIII
MAM
TM Cytoplasmic Domain
s
a1
a2
b1
b2
c

FIG. 1B

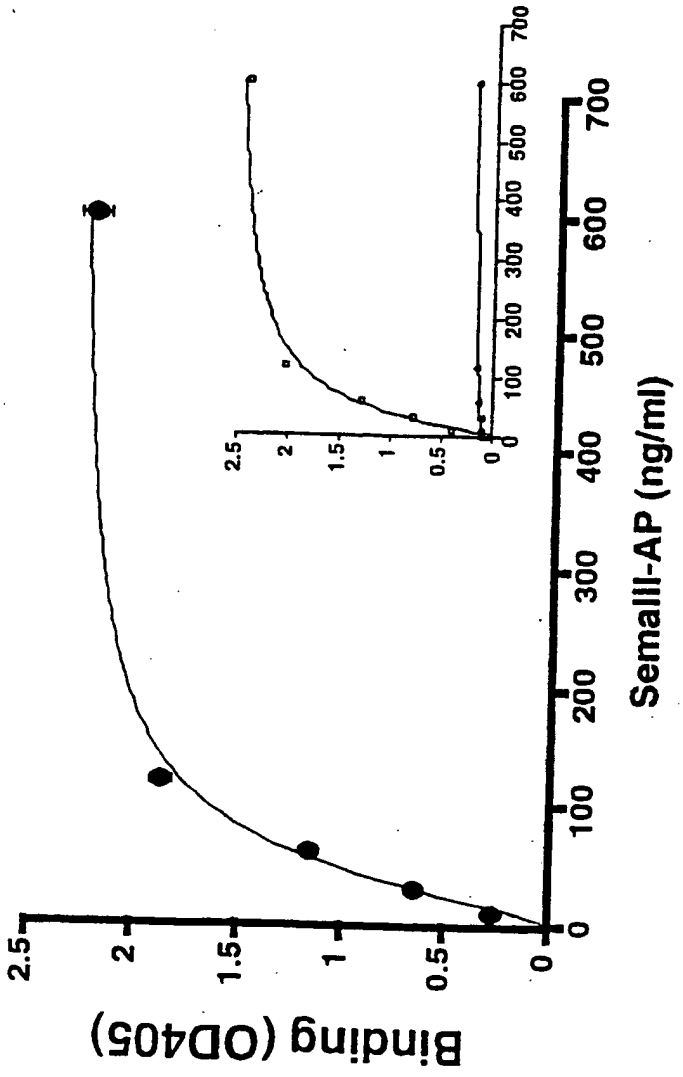
Binding (OD405)
2.5
2
1.5
1
0.5
0
0
100
200
300
400
500
600
700
SemaIII-AP (ng/ml)

FIG. 2A

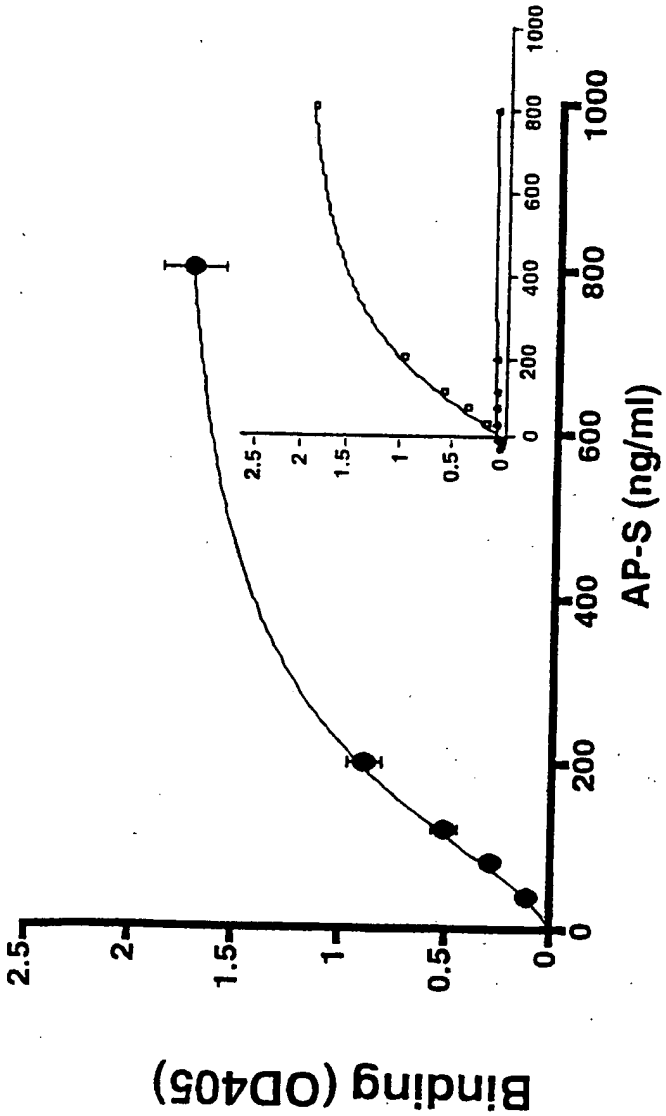
Binding (OD405)
2.5
2
1.5
1
0.5
0
0
200
400
600
800
1000
AP-S (ng/ml)
0
200
400
600
800
1000
0
0.5
1
1.5
2
2.5

FIG. 2B

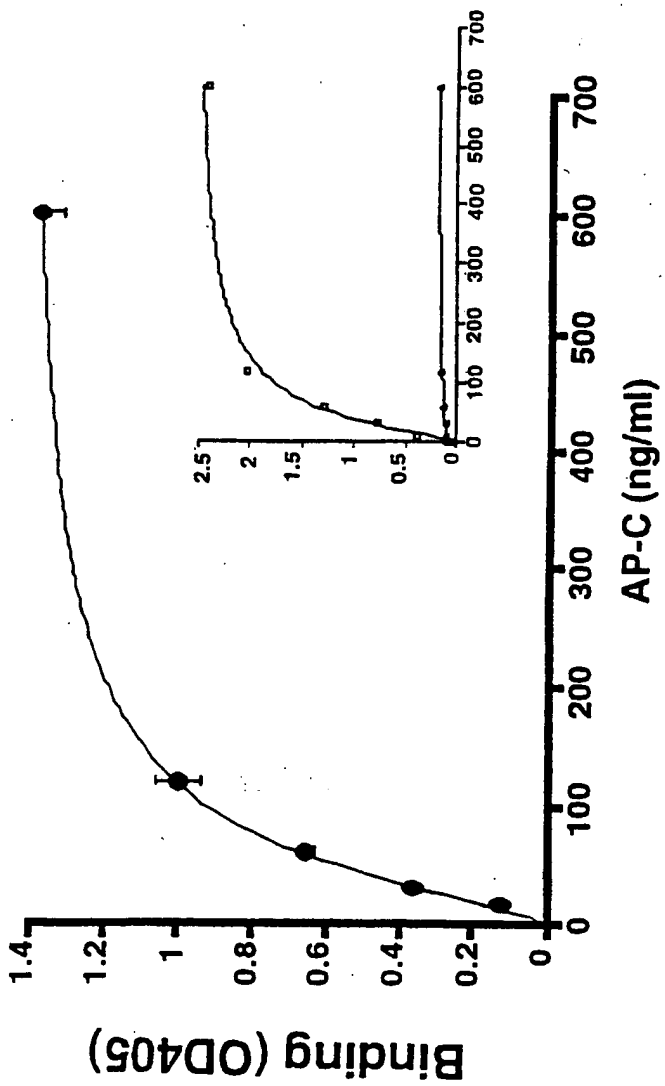
Binding (OD405)
1.4
1.2
1
0.8
0.6
0.4
0.2
0
0
100
200
300
400
500
600
700
AP-C (ng/ml)
2.5
2
1.5
1
0.5
0
0
100
200
300
400
500
600
700

FIG. 2C

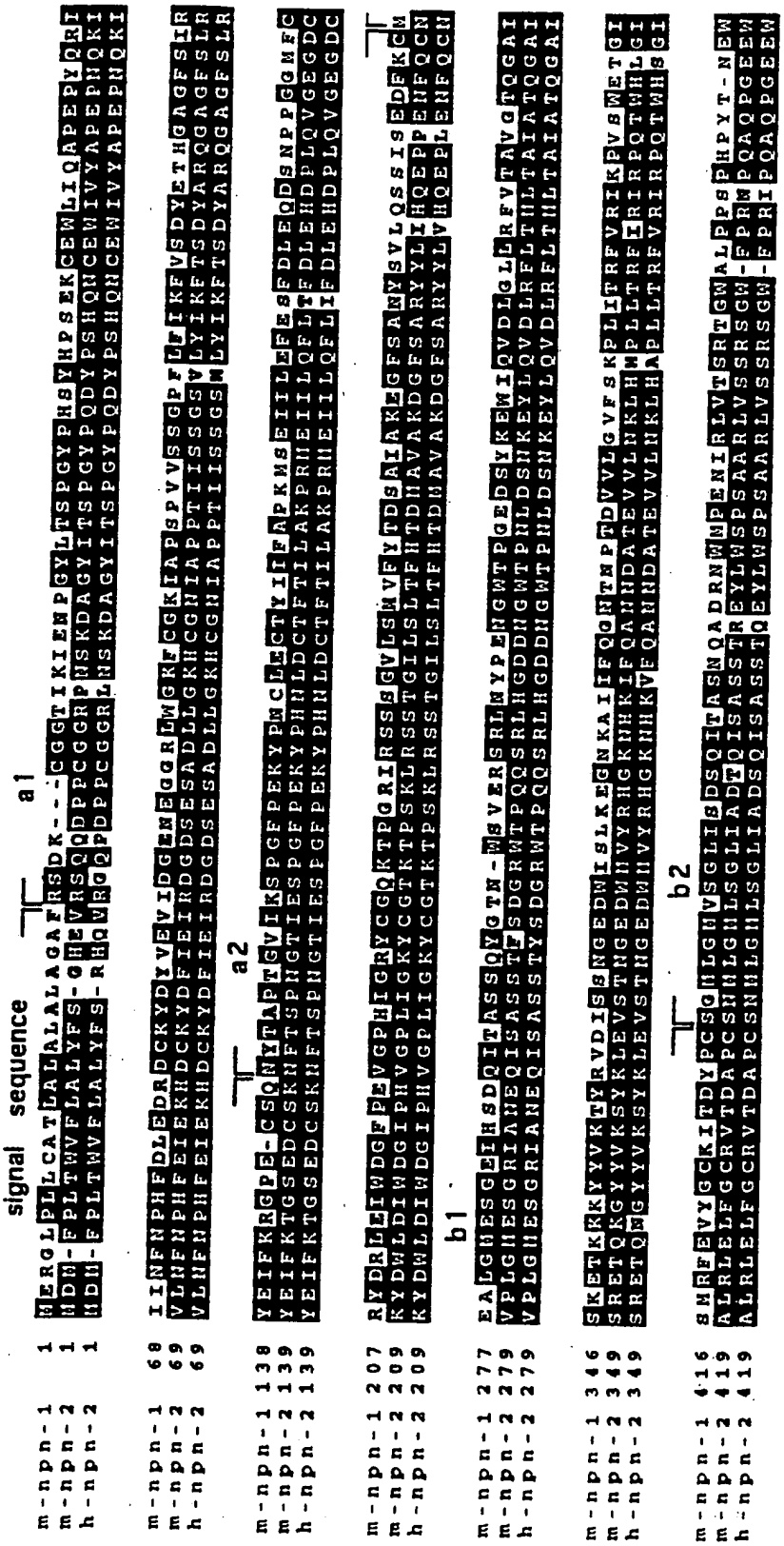

FIG. 3A